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(54) Title: A METHOD FOR TREATING HERPES VIRUSES

(57) Abstract: The present invention relates to a method for selecting an anti-herpes viral compound and a method for selectively inhibiting herpesvirus in a human host in need of such treatment. The present invention relates to a method for selecting an anti-herpes viral compound and a method for selectively inhibiting herpesvirus in a human host in need of such treatment.

A METHOD FOR TREATING HERPES VIRUSES

FIELD OF THE INVENTION

The present invention relates to a method for selecting an anti-herpes viral compound and a method for selectively inhibiting herpes viruses in a human host in need of such treatment.

BACKGROUND OF THE INVENTION

The herpesviruses comprise a large family of double stranded DNA viruses. Eight of the herpes viruses, herpes simplex virus types 1 and 2 (HSV-1 and HSV-2), varicella zoster virus (VZV), human cytomegalovirus (HCMV), Epstein-Barr virus (EBV), and human herpes viruses 6, 7, and 8 (HHV-6, HHV-7, and HHV-8), have been shown to infect humans. Several of these viruses are important human pathogens.

HSV-1 is estimated to affect 100 million people in the U.S. Primary infection of HSV-1 usually occurs between the ages of one and four. Cold sores, the visible symptom, typically appear at a later age, with 20-45% of the population over the age of fifteen affected (Whitley, Clin. Infect. Dis., 26:541-555, 1998).

Genital herpes (HSV-2) is the second most common sexually transmitted disease, with approximately 22% of the U.S population infected with this virus (Fleming 1997). VZV is the causative agent of chicken pox upon primary infection and can recur in adults as zoster.

EBV results in approximately two million cases of infectious mononucleosis in the U.S. each year. It can also cause lymphomas in immunocompromised patients and has been associated with Burkitt's lymphoma, nasopharyngeal carcinoma, and Hodgkins disease.

Infection with HCMV often occurs during childhood and is typically asymptomatic except in immunocompromised patients where it causes significant morbidity and mortality.

HHV-6 is the causitive agent of roseola and may be associated with multiple sclerosis and chronic fatigue syndrome. HHV-7 disease association is unclear, but it may be involved in some cases of roseola. HHV-8 has been associated with Karposi's sarcoma, body cavity based lymphomas, and multiple myeloma.

These viruses are capable of residing in a latent state within the host. Reactivation of latent virus results from response to environmental stimuli (ex. UV exposure, stress,

etc.). Infections or recurrence can be life threatening in immunocompromised patients such as AIDS or transplant patients where HCMV can result in retinitis, pneumonia, and gastrointestinal disease.

The increased immunocompromised population has created an unmet medical need
5 for antivirals against herpesviruses because current therapies do not have a sufficiently broad spectrum against this family of viruses and/or they have limited utility due to toxicity. The present invention provides a method for selectively inhibiting herpesviruses DNA polymerase with compounds that have broad spectrum activity. The method offers a distinct advantage in the treatment of patients in need, particularly immunocompromised
10 patients at risk of infection or reactivation by many members of the herpesvirus family.

SUMMARY OF THE INVENTION

The present invention provides a method of selecting compounds that inhibit herpes viruses comprising:

- 15 a) measuring IC₅₀ of a compound of interest that inhibits a wild type herpes virus,
- b) measuring IC₅₀ of the same compound that inhibits a binding domain mutant herpes virus which is the same strain of the wild type herpes virus,
- c) comparing IC₅₀ of step a with IC₅₀ of step b; and
- d) selecting the compound of interest wherein the IC₅₀ of step b is at least 3 times
20 greater than the IC₅₀ of step a.

In above method, the order of step a and step b are interchangeable.

The present invention further provides a method of selecting compounds that inhibit herpes viruses comprising:

- a) measuring IC₅₀ of a compound of interest that inhibits a wild type HSV-1,
- 25 b) measuring IC₅₀ of the same compound that inhibits a binding domain mutant HSV-1 which is the same strain of the wild type herpes virus,
- c) comparing IC₅₀ of step a with IC₅₀ of step b; and
- d) selecting the compound of interest wherein the IC₅₀ of step b is at least 3 times
30 greater than the IC₅₀ of step a.

In above method, the order of step a and step b are interchangeable.

The present invention further provides a method of selecting compounds that inhibit herpes viruses comprising:

- a) measuring IC₅₀ of a compound of interest that inhibits a wild type HSV-2,

- b) measuring IC_{50} of the same compound that inhibits a binding domain mutant HSV-2 which is the same strain of the wild type herpes virus,
- c) comparing IC_{50} of step a with IC_{50} of step b; and
- d) selecting the compound of interest wherein the IC_{50} of step b is at least 3 times greater than the IC_{50} of step a.

5 In above method, the order of step a and step b are interchangeable.

The present invention further provides a method of selecting compounds that inhibit herpes viruses comprising:

- a) measuring IC_{50} of a compound of interest that inhibits a wild type HCMV,
- 10 b) measuring IC_{50} of the same compound that inhibits a binding domain mutant HCMV which is the same strain of the wild type herpes virus,
- c) comparing IC_{50} of step a with IC_{50} of step b; and
- d) selecting the compound of interest wherein the IC_{50} of step b is at least 3 times greater than the IC_{50} of step a.

15 In above method, the order of step a and step b are interchangeable.

The present invention further provides a method for selectively treating diseases caused by herpes viruses in a human host comprising administering a compound to a human in need of such treatment wherein said compound inhibits herpes viruses by interaction with the binding domain in the viral DNA polymerase.

20 The present invention further provides method for selectively inhibiting herpes viruses in a human host comprising administering a compound to a human in need of such treatment wherein IC_{50} of the compound that inhibits a binding domain mutant herpes virus is at least 3 times greater than IC_{50} of the compound that inhibits a wild type herpes virus which is the same strain as the mutant herpes virus.

25 The present invention further provides a compound for treating herpesviral infections in a human host wherein IC_{50} of the compound that inhibits a binding domain mutant herpes virus is at least 5 times greater than IC_{50} of the compound that inhibits a wild type herpes virus which is the same strain as the mutant herpes virus.

The present invention further provides a compound for treating herpesviral infections in a human host wherein said compound inhibits the herpesvirus by interacting with the binding domain in the viral DNA polymerase.

The present invention further provides a compound for the inhibiting of herpesvirus DNA polymerases wherein serial passage of a wild type herpes virus in the presence of said

compound results in a change of the wild type HSV-1 polymerase at amino acid 823 from valine to alanine.

The present invention further provides a compound for inhibiting herpesvirus DNA polymerases wherein serial passage of a wild type herpes virus in the presence of said 5 compound results a change of the wild type HCMV polymerase at amino acid 823 from valine to alanine and at amino acid 824 from valine to leucine.

The present invention further provides a mutant herpesvirus DNA molecule having a nucleotide sequence selected from a group consisting of SEQ.ID.NO. 1; SEQ.ID.NO. 3; SEQ.ID.NO. 5; SEQ.ID.NO. 7; SEQ.ID.NO. 9; and SEQ.ID.NO. 11.

10 The present invention further provides a mutant herpesvirus polymerase amino acid molecule having an amino acid sequence selected from a group consisting of SEQ.ID.NO. 2; SEQ.ID.NO. 4; SEQ.ID.NO. 6; SEQ.ID.NO. 8; SEQ.ID.NO. 10 and SEQ.ID.NO. 12.

BRIEF DESCRIPTION OF THE DRAWINGS

15 Figure 1 – examples of 4-oxo-DHQ and 4-oxo-DHTP compounds.

Figure 2 – Herpesvirus' polymerases amino acid conserved region.

Figure 3 – Recovered virus after serial passage of HSV-1 in presence of 20 μ M of compound No. 17.

20 Figure 4 – Comparision of Wild HSV-1 and HSV-2 herpesvirus DNA polymerase amino acid sequences alligned by amino acid homology. (Seq. No: 14-19)

Figure 5 – Mutant Herpes Virus DNA and amino acid sequence list. (Seq. No: 1-12)

Figure 6 – Wild HCMV herpesvirus DNA polymerases amino acid sequence. (Seq. No 13)

25 DETAILED DESCRIPTION OF THE INVENTION

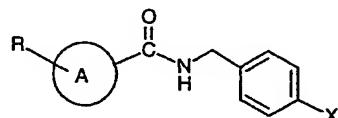
A key enzyme in the replication of all herpesviruses is the virus-coded DNA polymerase. Most of the currently available anti-herpes drugs target the viral DNA polymerase. Drugs such as Foscarnet acts by direct inhibition of the viral polymerase. These drugs are non-nucleoside inhibitors of herpesvirus DNA polymerases. Others such as the 30 nucleoside analogs, Acyclovir, Penciclovir and Ganciclovir must first be phosphorylated to the monophosphate forms by virus encoded kinases and, further phosphorylated to triphosphate by cellular enzymes before they are active inhibitors. The triphosphate forms of these nucleoside analogs inhibit polymerases by competing with the binding of natural

triphosphates and their subsequent insertion into growing DNA strands. These drugs are known as nucleoside inhibitors of herpesvirus DNA polymerases.

One of the limitations of the currently available drugs is that they are active against only a few of the eight human herpesviruses. For example, Acyclovir and Penciclovir 5 inhibit HSV and VZV replication but have poor activity against CMV.

In order to identify antiviral compounds that would have the potential to inhibit replication of most of the human herpesviruses, compounds are *in vitro* screened for inhibitors of herpesvirus DNA polymerase activity. Because portions of the amino acid sequence of the polymerases are highly conserved within the herpesvirus family it is 10 possible to discover small molecules that inhibit herpesvirus polymerases but not cellular DNA polymerases. Using this biochemical approach, several new classes of compounds such as the 4-hydroxyquinoline derivatives (4-HQ), 4-oxo-dihydroquinoline derivatives (4-oxo-DHQ) and 4-oxo-dihydrothienopyridine derivatives (4-oxo-DHTP) were discovered as potent, non-nucleoside herpesvirus DNA polymerase inhibitors. *In vitro* polymerase assays 15 and/or *in vivo* cell culture assays have demonstrated that these compounds inhibit HSV-1, HSV-2, HCMV, VZV, EBV, and HHV-8 replication.

4-Oxo-DHQ and 4-oxo-DHTP are derivatives of formula I



I

20 wherein ring A is a saturated or unsaturated fused double or triple heterocyclic ring having 1, 2, 3 or 4 heteroatoms selected from group consisting of oxygen, sulfur, or nitrogen; and wherein R and X are the appropriated substitutents, respectively.

Examples of 4-HQ compounds, 4-oxo-DHQ compounds and 4-oxo-DHTP compounds are illustrated in Figure 1.

25 Antiviral activity of these examples are shown in Table 1 below. As shown in Table 1, these compounds inhibit HSV-1 and HSV-2 as well or better than the current commercially available drug Acyclovir.

Table 1

Antiviral Activity of 4-oxo DHQ/4-oxo DTHP Against HSV-1 and HSV-2

virus	Compound IC ₅₀ (uM)					
	1	2	3	4	5	ACV
HSV-1 KOS	2.0	3.8	3.2	3.2	3.3	3.6
HSV-1 F	2.5	2.3	2.2	2.1	2.6	1.3
HSV-1 DJL	2.5	2.6	1.8	2.2	2.7	1.8
HSV-1 Patton	ND	5.3	7.7	4.3	10	9.3
HSV-2 MS	2.0	2.5	2.8	2.5	2.5	10
HSV-2 35D	ND	5.4	5.0	3.2	8.1	6.0
HSV-2 186	2.0	2.3	3.2	2.3	4.2	>10

5 It has also been discovered that point mutations within the HSV-1 polymerase gene that confer resistance to Acyclovir and other nucleoside analogs do not result in resistance to the 4-HQ, 4-oxo-DHQs or 4-oxo-DHTPs. Serial passage of wild type HSV-1 in the presence of 4-oxo-DHQ results in the isolation of mutants that are highly resistant (>20 fold increase in the IC₅₀) to these compounds while retaining sensitivity to nucleoside inhibitors

10 such as Acyclovir.

In order to determine the mechanism of action of 4-HQ, 4-oxo-DHQ and 4-oxo-DHTP compounds against herpes viruses, mutants resistant to these compounds are isolated by serial passage of the virus in the presence of a 4-oxo-DHQ compound. Sequencing analysis of HSV-1 and HSV-2 strains resistant to the 4-oxo-DHQ identifies that HSV-1

15 (KOS strain) polymerase protein and its homologous HSV-2 have a conserved region (a binding domain), which is a critical contact point for these compounds. While amino acid numbering of the DNA polymerase may vary between strains of HSV-1 and HSV-2, this binding domain encompassing the HSV-1 (KOS) strain amino acid 823 is highly conserved in herpesviruses and can be identified by aligning the homologous amino acids of this

20 domain as shown in Fig 2.

In HSV-1 and HSV-2 strains resistant to the 4-oxo-DHQ and similar compounds, a change of valine to an alanine at the binding domain provides full resistance.

In the HSV-1 DNA polymerase, resistance is also found when a valine changes to methionine at amino acid 823 but only when accompanied by a second amino acid change.

25 Isolation of HCMV resistant to 4-oxo-DHQ's is found to be very difficult. Comparison of the amino acid sequence of the HSV polymerase (Y-G-F-T-G-V-Q-H-G) and HCMV polymerase (Y-G-F-T-G-V-V-N-G) in the region of amino acid 823 (underlined amino acid) shows that there is a second valine at position 824 in the HCMV

polymerase. In vitro assay using mutant HCMV polymerases demonstrates that full resistance to the 4-oxo-DHQs requires changes at both amino acids 823 (a valine to alanine) and 824 (a valine to leucine). A HCMV polymerase gene containing V823A and V824L mutations is used in marker rescue experiments to generate a viral mutant. This mutant has 5 an IC₅₀ approximately 7-fold above that of wild-type HCMV.

The HSV-1, HSV-2 and HCMV mutants are also found to be resistant to other non-nucleoside inhibitors such as the 4-oxo-DHTP and similar compounds. However, when the binding domain mutants (e. g. HSV-1 V823A, HSV-2-MS V826A, HSV-2-186 V828A, and HCMV V823A/V824L mutants) are tested in plaque reduction assays against a series of 10 nucleoside polymerase inhibitors and the non-nucleoside inhibitor such as Foscarnet, replication of the mutants is found to be inhibited by all of the currently marketed anti-herpes polymerase inhibitors tested.

These studies demonstrate that certain non-nucleosides like 4-HQ, 4-oxo-DHQ and 4-oxo-DHTP compounds bind to a different site on the herpes polymerase than the 15 nucleoside inhibitors and Foscarnet. The valine at the binding domain is conserved in the DNA polymerases of six of the eight human herpesviruses and several animal herpesviruses, and appears to play a critical role in the antiviral activity of the 4-HQ, 4-oxo-DHQ and 4-oxo-DHTP compounds. (See Figure 2)

Since mutation at the binding domain negates these non-nucleoside inhibitors' 20 activities, compounds could be tested against wild type polymerases and the mutant polymerases to establish the probability of similar binding. We refer to this property of compounds as interaction with the binding domain. Since compounds that interact with the binding domain have exhibited broad-spectrum activity against herpesviruses, this invention provides a method for selecting compounds to treat individuals such as 25 immunocompromised patients who are afflicted with multiple herpesvirus infections.

Definitions

The term "wild-type" refers to a gene or gene product which has the characteristics of that gene or gene product when isolated from a naturally occurring source. A wild-type 30 gene is that which is most frequently observed in a population and is thus arbitrarily designated the "normal" or "wild-type" form of the gene.

In contrast, the term "mutant" refers to a gene or gene product which displays modifications in sequence and or functional properties (i.e., altered characteristics) when

compared to the wild-type gene or gene product. It is noted that naturally-occurring mutants can be isolated; these are identified by the fact that they have altered characteristics when compared to the wild-type gene or gene product.

IC₅₀ refers to concentration of a drug that inhibits virus growth by 50%.

5 Wild type HSV-1 and HSV-2 strains are listed in Figure 4.

Wild type HCMV is listed in SEQ. ID. NO.13.

The term "Iudr" refers to antiviral drug Iododeoxyuridine.

The term "BvdU" refers to antiviral drug Bromovinyldeoxyuridine.

The term "ACV" refers to antiviral drug Acyclovir.

10 The term "AraC" refers to antiviral drug Arabinosylcytidine.

The term "AraT" refers to antiviral drug Arabinosylthymine.

The term "AraA" refers to antiviral drug Arabinosyladenine.

The term "GCV" refers to antiviral drug Ganciclovir.

The term "CDV" refers to antiviral drug Cidofovir.

15 The term "PFA" refers to antiviral drug Foscarnet.

The term "binding domain" refers to a conserved region in herpesvirus DNA polymerases. The herpesvirus DNA polymerases have seven (7) conserved regions. The binding domain is within the third conserved region (see Figure 2). When the binding domain contacts with an inhibitor, at least one amino acid in the binding domain mutates and provides the resistance. In general, the binding domain is at an amino acid sequence position 818-829 of the HSV-1 DNA polymerase or the homologous region in other herpes virus DNA polymerases (see Figure 2).

The term "a binding domain mutant herpes virus" refers to a herpes virus containing a binding domain mutation.

25 More specifically, the binding domain in HSV-1 strains, KOS, F, DJL and Patton are at amino acid sequence position 823. The binding domain in HSV-2 MS-M1 strain is at amino acid sequence position 826. The binding domain in HSV-2 186 strain is at amino acid sequence position 828. The binding domain in HCMV AD 169 strains is at amino acid sequence position 823-824.

30 The term "XxxY" refers to an amino acid sequence position xxx, a single amino acid X in wild type is changed to an amino acid Y.

For example, the term "V823A" refers to an amino acid sequence position 823, a Valine found in wild type is changed to alanine in mutant strain.

The term "V824L" refers to an amino acid sequence position 824, a Valine found in wild type is changed to Leucine in mutant strain.

The term "V826A" refers to an amino acid sequence position 826, a Valine found in wild type is change to alanine in mutant strain.

5 The term "V828A" refers to an amino acid sequence position 828, a Valine found in wild type is change to alanine in mutant strain.

A table of amino acids and their representative abbreviations, symbols and codons is set forth below in the following Table.

10

Amino acid	Abbrev.	Symbol	Codon(s)					
Alanine	Ala	A	GCA	GCC	GCG	GCU		
Cysteine	Cys	C	UGC	UGU				
Aspartic acid	Asp	D	GAC	GAU				
Glutamic acid	Glu	E	GAA	GAG				
Phenylalanine	Phe	F	UUC	UUU				
Glycine	Gly	G	GGA	GGC	GGG	GGU		
Histidine	His	H	CAC	CAU				
Isoleucine	Ile	I	AUA	AUC	AAU			
Lysine	Lys	K	AAA	AAG				
Leucine	Leu	L	UUA	UUG	CUA	CUC	CUG	CUU
Methionine	Met	M	AUG					
Asparagine	Asn	N	AAC	AAU				
Proline	Pro	P	CCA	CCC	CCG	CCU		
Glutamine	Gln	Q	CAA	CAG				
Arginine	Arg	R	AGA	AGG	CGA	CGC	CGG	CGU
Serine	Ser	S	AGC	AGU	UCA	UCC	UCG	UCU
Threonine	Thr	T	ACA	ACC	ACG	ACU		
Valine	Val	V	GUU	GUC	GUG	GUU		
Tryptophan	Trp	W	UGG					
Tyrosine	Tyr	Y	UAC	UAU				

MATERIALS AND METHODS

Cell and Viruses

African green monkey kidney cells (Vero) and human foreskin fibroblast cells (HFF) and herpes viruses can be obtained from the American Type Culture Collection (ATCC). Media is defined as Dulbecco's modified Eagle media (DMEM) containing 10% fetal bovine serum (FBS) and supplemented with antibiotics. Cells are maintained in media at 37°C in a humidified atmosphere of 5% CO₂. HSV-1 strains F, Patton and DJL, HSV-2 strains MS, 35D and 186, and HCMV strain AD169 are used in these studies. Strain DJL is 15 a clinical isolate of HSV-1 isolated in our lab from a primary oral lesion.

20

Measuring IC₅₀ of a Compound of Interest That Inhibits Herpes Viruses

Preparation of Virus Stocks: HSV-1 and HSV-2 stocks are grown in Vero cells. HCMV stocks are grown in HFF cells. Approximately 1 ml of media containing sufficient virus to infect approximately 0.1% to 1% of the cells (multiplicity of infection of 0.001 to 5 0.01 PFU/cell) is added to a T-150 cell culture flask containing a confluent monolayer of cells. The cells are incubated at 37°C for approximately 1 hour. Approximately 50 ml of media is then added to the flask and the cells are incubated at 37°C until viral cytopathic effect (cpe) is apparent in 100% of the cells. The flask is then placed at -80°C for at least 30 min. The flask containing frozen media and cells is placed in a 37°C water bath until the 10 media is thawed. This process disrupts the cells and releases virus into the media. 1 ml aliquots of media containing virus are dispensed into tubes and stored at -80°C. These aliquots of media containing virus are referred to as virus stocks.

Titrating Virus Stocks: Aliquots of virus are thawed at 37°C and serially diluted (10 fold dilutions) in media. 0.1 ml of each dilution of virus is placed in a single well of 24- 15 well cell culture dish containing a confluent monolayer of cells (Vero cells for HSV-1 and HSV-2, HFF cells for HCMV) and incubated at 37°C for 1 h. The virus inoculum is then removed and 1 ml of media containing 0.8% carboxymethylcellulose (CMC) is added to each well of the dish. The dish is incubated at 37°C for approximately 2-3 days (HSV-1 and HSV-2) or 6-9 days (HCMV) to allow sufficient growth of virus to form plaques in the 20 cell monolayer. Plaques can be observed and counted microscopically or by staining the cells with 0.1% crystal violet in 20% ethanol. The virus titer which is expressed as plaque forming units (PFU) per ml is obtained by counting the plaques in a well and correcting for the dilution of the viral inoculum.

Plaque Reduction Assays: Antiviral activity of compounds against herpesviruses such as 25 HSV-1, HSV-2, or HCMV can be measured using plaque reduction assays. 0.1 ml of media containing approximately 50 PFU of virus is added to each well of a 24-well cell culture dish containing a confluent monolayer of cells (Vero cells for HSV-1 and HSV-2, HFF cells for HCMV). Compounds are dissolved in 100% DMSO and diluted in 100% DMSO as 200x stocks of the desired final drug concentration. Typically 5-6 two-fold dilutions are 30 prepared for each compound. Dilutions of compounds are then added to media containing 0.8% CMC resulting in a final 1x drug concentration. After the virus-infected cells have incubated for 1 h at 37°C, the virus inoculum is removed and 1 ml of media containing 0.8% CMC and the various concentrations of compound is added to each well of the dish.

The dish is incubated at 37°C for approximately 2-3 days (HSV-1 and HSV-2) or 6-9 days (HCMV) to allow sufficient growth of virus to form plaques in the cell monolayer. Plaques can be observed and counted microscopically or by staining the cells with 0.1% crystal violet in 20% ethanol. Virus inhibition is determined for each drug concentration by 5 comparing the number of plaques in drug-containing wells to control wells that did not contain drug. Antiviral activity of a compound is expressed as the concentration of compound predicted to reduce the number of plaques in a well by 50% (IC₅₀). The IC₅₀ values are calculated by plotting the per cent inhibition vs. concentration of compound using EXCEL software for linear regression.

10

Selection of 4-oxo-DHQ resistant HSV-1 and HSV-2

Vero cells are plated out at a density of 3.5×10^5 cells per well in a six well tissue culture plate. Cells are infected with HSV-1 KOS at a multiplicity of infection (moi) of 0.1 pfu/cell and 1 h post infection the cells are overlayed with 3 ml media containing 20 15 uM of a 4-oxo-DHQ. Cultures are incubated for 20 h at 37°C, freeze/thawed to release cell-associated virus, and 0.1 ml of culture is used to infect a new monolayer of Vero cells (one passage). Serial passage is repeated seven times in the presence of 20 uM drug. Virus isolates are then plaque purified three times prior to preparation of stocks. Virus recovered from each passage in the presence of compound No. 17 is shown in Figure 3. 4-oxo-DHQ 20 resistant HSV-1 and HSV-2 may also be selected by the marker transfer method described below using wild-type HSV DNA and the corresponding mutant HSV polymerase gene.

Marker Transfer of a HCMV Mutation

A plasmid containing the wild-type HCMV polymerase gene is modified to contain 25 the V823A or V823A and V824L mutations using a site-directed mutagenesis Kit (Stratagene Corp.) and following the manufacturer's protocol. HFF cells are plated into T25 tissue culture flasks to achieve 80% confluence at the time of the transfection. Wild type HCMV AD169 DNA and plasmid DNA containing the mutant HCMV polymerase gene are mixed at a ratio of 1:2 (2ug of viral DNA to 4 ug of plasmid DNA). DNA's are 30 transfected using superfect transfection reagent according to methods recommended by the manufacturer (Qiagen Inc.). Cells are harvested five days posttransfection, freeze-thawed to release virus and half of the sample is used to infect HFF cell monolayers. Cells are overlayed with media containing 20 uM 4-oxo-DHQ compound 2 (see Figure 1). Serial

passage is repeated seven times in the presence of 20 uM compound 2 and virus isolates are then plaque purified three times prior to preparation of viral stock.

Isolation of HSV and HCMV viral DNA

5 HSV DNA is purified from the cytoplasm of infected Vero cells. Vero cells (50 % confluent) are infected at an multiplicity of 0.01 PFU/cell. At 3-5 days postinfection infected cells (100% cpe) are harvested by centrifugation at 1000 rpm in a Beckman GS-6R centrifuge. The pelleted cells are resuspended in TE buffer and placed on ice for 15 minutes. NP-40 is then added to a final concentration of 0.2% and incubated on ice for a

10 further 15 minutes. The cells are centrifuged at 2000 rpm for 10 minutes in a Beckman GS-6R centrifuge. The supernatant is removed and EDTA is added to a final concentration of 20 mM followed by the addition of SDS to a final concentration of 0.3% and proteinase K to a concentration of 50 ug/ml then incubated at 45C for 2 hours. HCMV DNA is isolated by infecting HFF cells (25% confluency) with HCMV at an multiplicity of 0.1 PFU/cell.

15 Cells and media are harvested 5-7 days postinfection (100% cpe) and subjected to low speed centrifugation to remove intact cells and cell debris followed by a high speed spin to pellet virus particles (2500 rpm's in a Beckman SW28 rotor for 1 hour). Following incubation of the HSV and HCMV samples, 1.5 volumes of saturated NaI is added to the digested extract and the refractive index is adjusted to 1.434 – 1.435. Ethidium bromide is

20 added to a final concentration of 50 ug/ml. The samples are loaded into a VTI 50centrifuge tube and spun for 24 hours at 45,000 rpm. The DNA band is harvested extracted three times with n-butanol, then dialyzed against TE buffer followed by a dialysis against 95% ethanol and a final dialysis against TE buffer.

25 **DNA Sequencing**

HSV-1, HSV-2 or HCMV viral DNA's are sequenced directly using an ABI377 fluorescence sequencer (Perkin Elmer Applied Biosystems, Foster City, CA) and the ABI BigDye PRISMTM dRhodamine Terminator Cycle Sequencing Ready Reaction Kit with AmpliTaq FSTM DNA polymerase (PE Applied Biosystems). Each cycle sequencing reaction contained about 1.0 ug of purified viral DNA. Cycle-sequencing is performed using an initial denaturation at 98°C for 1 min, followed by 50 cycles: 98°C for 30 sec, annealing at 50°C for 30 sec, and extension at 60°C for 4 min. Temperature cycles and times are controlled by a Perkin-Elmer 9700 thermocycler. Extension products are

purified using Centriflex™ gel filtration cartridges (Edge BioSystems, Gaithersburg, MD). Each reaction product is loaded by pipette onto the column, which is then centrifuged in a swinging bucket centrifuge (Sorvall model RT6000B table top centrifuge) at 750 x g for 1.5 min at room temperature. Column-purified samples are dried under vacuum for about 40 5 min and then dissolved in 4 ul of a DNA loading solution (83% deionized formamide, 8.3 mM EDTA, and 1.6 mg/ml Blue Dextran). The samples are then heated to 90°C for two min, and held at 4°C until loading. 1.5 ul of each sample is loaded into a single well of the ABI377 sequencer. Sequence chromatogram data files from the ABI377 are analyzed with the computer program Sequencher (Gene Codes, Ann Arbor, MI), for assembly of sequence 10 fragments and correction of ambiguous base calls. Generally sequence reads of 600-700 bp are obtained. Potential sequencing errors are minimized by obtaining sequence information from both DNA strands and by re-sequencing difficult areas using primers at different locations until all sequencing ambiguities are removed.

The entire coding region of the polymerase genes from both the parent strains and 15 the resistant viruses are sequenced. The DNA sequencing is done using viral DNA as the template thus avoiding cloning of the polymerase genes. The amino acid sequence of the DNA polymerases of HSV-1 KOS, F, Patton and DJL and HSV-2 MS and 186 are compared in **Figure 4**. Amino acids that are identical for the six polymerases are shaded in black while regions where amino acid differences are found are shaded in gray. The amino 20 acid sequence of the four HSV-1 polymerases are essentially identical with only a few minor changes noted between the different HSV-1 strains. The majority of amino acid changes are found when the sequences of the HSV-1 and HSV-2 polymerases are compared.

25 **Isolation and Characterization of HSV-1 and HSV-2 Mutants That Are Resistant To the 4-oxo-DHQ's and 4-oxo-DHTP Compounds**

A panel of viruses consisting of four strains of HSV-1 (KOS, F, DJL, Patton) and three strains of HSV-2 (MS, 35D, 186) are tested in a plaque reduction assay against four different 4-oxo-DHQ compounds (# 1, 2, 4, 5 as shown in **Figure 1**), and one 4-oxo-DHTP 30 compound (# 3 as shown in **Figure 1**) and against Acyclovir. The six drugs inhibited replication of the seven virus strains with IC₅₀ values ranging from 2-10 µM (Table 1). In order to select for 4-oxo-DHQ resistant mutants, HSV-1 strains KOS, F, and DJL along with HSV-2 strains 186 and MS are serially passaged in the presence of 20 uM compound

1. Following the seventh passage, 4-oxo-DHQ resistant virus from each strain are plaque purified three times and high-titer stocks are made. All of the resistant HSV mutants grew to high titers in Vero cells, indicating that the mutations in the resistant isolates did not significantly impair their growth. The mutants selected with 4-oxo-DHQ compound 1
5 exhibited >10 fold increase in IC₅₀ when tested in a plaque reduction assay against 4-oxo-DHQ compound 1 Data are shown in Table 2.

Table 2
4-oxo-DHQ Resistant Virus of HSV-1 and HSV-2

Virus Mutants	Compound 1 IC ₅₀ (uM)	Amino Acid Change in HSV DNA Polymerase
HSV-1 Kos-M1	>20	- V823A
HSV-1 F-M1	>20	- V823A
HSV-1 DJL-M1	>20	-V823A
HSV-2 MS-M1	>20	- V826A
HSV-2 186-M1	>20	- V828A

10 *HSV-1 and HSV-2 isolates grown in the presence of 4-oxo-DHQ select for resistant virus.
DNA sequence analysis of the 4-oxo-DHQ resistant mutants (HSV-1 KOS-M1, HSV-1 F-M1, HSV-1 DJL-M1, HSV-2 186-M1, HSV-2 MS-M1) demonstrated that all five mutants contained a single point mutation of T to C at the binding domain resulting in a Valine to Alanine amino acid change.

15 **Isolation and Characterization of A HCMV Mutant That Is Resistant to The 4-oxo-DHQ's and 4-oxo-DHTP Compounds**
In order to select for a 4-oxo-DHQ HCMV resistant mutant, virus (strain AD169) is serially passaged in the presence of 20 uM a 4-oxo-DHQ. Although we could readily select
20 for HSV mutants using this procedure we failed to isolate an HCMV mutant, even when the virus is passaged at low drug concentrations (<5 uM). Comparison of the amino acid sequence of the HSV polymerase, Y-G-F-T-G-V-Q-H-G, and HCMV polymerase, Y-G-F-T-G-V-V-N-G, in the region of amino acid 823 (underlined amino acid) showed that there is a second valine at position 824 in the HCMV polymerase. In order to determine if both
25 valines need to be changed in order to confer resistance to the 4-oxo-DHQ's, *in vitro* polymerase assays are done using mutant HCMV polymerases containing either V823A or V823A plus V824L (Table 3).

Table 3
HCMV Mutant Polymerase Exhibits Resistance to 4-oxo-DHQ*

5

Polymerase	Compound 1 IC ₅₀ (μM)
HCMV (wild)	4.6
HCMV V823A	17.2
HCMV V823A/V824L	42.9

*Generation of the valine to alanine at amino acid 823 of HCMV results in a 3.5-fold increase in resistance.

*Mutation of the amino acid from valine to alanine and amino acid 824 from valine to leucine results in an 9-fold increase in resistance, relative to wild type.

10 The V823A alone resulted in a 3.5-fold increase in the IC₅₀ while the polymerase with the double amino acid change had nearly 10-fold increase in the IC₅₀. In order to isolate an HCMV resistant mutant marker rescue experiments are done. Plasmids containing the mutant polymerase genes are transfected into HFF cells along with wild type HCMV AD169 DNA. The resulting virus is then serially passaged in the presence of 20

15 uM compound 1 (see figure 1). A 4-oxo-DHQ resistant virus is isolated from marker rescue studies done with the HCMV polymerase gene containing mutations that result in the V823A, V824L amino acid changes, but not with the gene containing V823A change alone. The mutant selected with compound 1 (HCMV AD169-M1) exhibited ~7-fold increase in IC₅₀ when tested in a plaque reduction assay compared to Ganciclovir and

20 Cidofovir which has a ≤ 2-fold change in sensitivity (Table 4).

Table 4
Plaque reduction assay of 4-oxo-DHQ resistant HCMV*

Drug	HCMV AD169 IC ₅₀ (μM)	HCMV AD169 - M1 IC ₅₀ (μM)
Compound 1	0.7	4.7
Ganciclovir	0.9	1.0
Cidofovir	0.3	0.6

25 *Recombination of wild-type HCMV with a polymerase gene containing the valine to alanine at amino acid 823 and the valine to leucine at amino acid 824 allowed for selection of resistant virus with about 7-fold less sensitivity to compound 1.

*Sensitivity of resistant HCMV virus to Ganciclovir and Cidofovir verifies that the 4-oxo-DHQ's mechanism for inhibiting the polymerase protein is unique

The entire coding region of the HCMV polymerase genes from both the parent strain and the resistant virus are sequenced. The DNA sequencing is again done using viral DNA as the template thus avoiding cloning of the polymerase genes. Comparison of the DNA sequence of the two polymerase genes demonstrated that the resistant mutant 5 contained two point mutations that resulted in the predicted V823A, V824L amino acid changes. As with the HSV resistant viruses these results demonstrate the critical role of the region encompassing amino acid 823 for inhibition of polymerase activity by these compounds.

10 **Antiviral Activity of Nucleoside and Non-Nucleoside Polymerase Inhibitors Against 4-oxo-DHQ Resistant Mutants**

In order to determine if the 4-HQ binding domain mutations alter the sensitivity of the HSV-1, HSV-2 and HCMV mutants to both non-nucleoside (4-oxo-DHQ's) and nucleoside inhibitors (e.g Acyclovir and ganciclovir) several of the mutants are tested in 15 plaque reduction assays against a series of non-nucleoside compounds including Foscarnet (PFA), 4-HQ's 4-oxo-DHQ's and 4-oxo-DHTP's (Table 5). The mutants are also tested against a series of nucleoside inhibitors including acyclovir and ganciclovir (Table 5). The activity of these compounds against the mutants is compared to their activity against the wild type strains that are used to isolate the HSV and HCMV mutants. When tested against 20 a number of 4-HQ's, 4-oxo-DHQ's and 4-oxo-DHTP's and other related classes of compounds all of the drugs are found to inhibit the wild type virus with IC₅₀ values ranging from <0.1 uM to 30 uM. When these drugs are tested against the resistant viruses they are found to have IC₅₀ values 5 to 10 fold higher then the parent virus. There is little if any difference in the IC₅₀ values of the nucleoside compounds and the non-nucleoside PFA 25 between the wild type and mutant HSV-1, HSV-2, and HCMV viruses. These results demonstrate that the amino acid change in the binding domain (V823A in the HSV-1 polymerase, V826A in the HSV2-MS polymerase, V828A in the HSV2-186 polymerase, and the V823A/V824L changes in the HCMV polymerase) resulted in resistance to the 4-oxo-DHQ's and 4-oxo-DHTP's, which provides further evidence that these classes of 30 compounds share an affinity for a region we refer to as the binding domain. In contrast, these amino acid changes did not alter the activity of these viruses to other classes of polymerase inhibitors.

Table 5

Antiviral activity of nucleoside and non-nucleoside polymerase inhibitors
against HSV-1, HSV-2, and HCMV Isolates selected for 4-oxo-DHQ resistance*

Drug	Plaque Reduction Assay - IC ₅₀ (μM)					
	HSV-2 MS	HSV-2 MS-M1	HSV-1 KOS	HSV-1 KOS-M1	HCMV AD169	HCMV AD169-M1
6	28.8	>50	24.6	>50	5.1	>16
7	8.8	27.9	6.5	>50	0.3	3.4
8	2.3	>50	5.1	>50	<0.1	1.1
9	0.9	48.7	1.9	>50	<0.1	3.1
10	29.2	>50	15.8	>50	1.1	>16
11	3.0	>50	3.1	>50	0.7	3.9
12	0.4	12.5	1.3	>50	0.2	1.1
13	5.3	>50	5.5	<25	2.7	>16
14	1.6	>50	28.4	>50	0.9	18.4
2	1.3	>50	3.3	>50	0.4	4.0
4	2.1	28.4	4.2	>50	0.6	2.1
3	0.8	>50	4.0	>50	1.5	6.2
15	5.9	>50	>50	>50	0.7	7.7
Iudr	5.0	6.1	1.1	0.8	ND	ND
Bvdu	5.8	5.9	2.1	0.1	ND	ND
ACV	2.4	2.8	3.9	4.4	ND	ND
AraC	0.2	0.1	0.2	0.2	ND	ND
AraT	6.6	3.6	11.6	3.6	ND	ND
AraA	10.6	18.2	26.1	27.2	ND	ND
GCVir	ND	ND	ND	ND	0.8	0.8
CDV	ND	ND	ND	ND	0.4	0.3
PFA	ND	ND	ND	ND	38	<20

5 *HSV-2 MS, HSV-1 KOS, HCMV AD169: wild type strains

*HSV-2 MS-M1, HSV-1 KOS-M1, HCMV AD169-M1: mutants selected for 4-oxo-DHQ resistance

*ND - Not Done.

Antiviral compounds identified by the present invention can conveniently be
10 administered in a pharmaceutical composition containing the compound in combination
with a suitable excipient, the composition being useful in combating viral infections.
Pharmaceutical compositions containing a compound appropriate for antiviral use are
prepared by methods and contain excipients which are well known in the art. A generally
recognized compendium of such methods and ingredients is Remington's Pharmaceutical
15 Sciences by E.W. Martin (Mark Publ. Co., 15th Ed., 1975).

Antiviral compounds identified by the present invention and their compositions can
be administered parenterally (for example, by intravenous, intraperitoneal or intramuscular

injection), topically, orally, or rectally, depending on whether the preparation is used to treat internal or external viral infections.

For oral therapeutic administration, the active compound may be combined with one or more excipients and used in the form of ingestible tablets, buccal tablets, troches, 5 capsules, elixirs, suspensions, syrups, wafers, and the like. Such compositions and preparations should contain at least 0.1% of active compound. The percentage of the compositions and preparations may, of course, be varied and may conveniently be between about 2 to about 60% of the weight of a given unit dosage form. The amount of active compound in such therapeutically useful compositions is such that an effective dosage level 10 will be obtained.

The tablets, troches, pills, capsules, and the like may also contain the following: binders such as gum tragacanth, acacia, corn starch or gelatin; excipients such as dicalcium phosphate; a disintegrating agent such as corn starch, potato starch, alginic acid and the like; a lubricant such as magnesium stearate; and a sweetening agent such as sucrose, 15 fructose, lactose or aspartame or a flavoring agent such as peppermint, oil of wintergreen, or cherry flavoring may be added. When the unit dosage form is a capsule, it may contain, in addition to materials of the above type, a liquid carrier, such as a vegetable oil or a polyethylene glycol. Various other materials may be present as coatings or to otherwise modify the physical form of the solid unit dosage form. For instance, tablets, pills, or 20 capsules may be coated with gelatin, wax, shellac or sugar and the like. A syrup or elixir may contain the active compound, sucrose or fructose as a sweetening agent, methyl and propylparabens as preservatives, a dye and flavoring such as cherry or orange flavor. Of course, any material used in preparing any unit dosage form should be pharmaceutically acceptable and substantially non-toxic in the amounts employed. In addition, the active 25 compound may be incorporated into sustained-release preparations and devices.

Antiviral compounds identified by the present invention and their compositions can also be administered intravenously or intraperitoneally by infusion or injection. Solutions of the active compound or its salts can be prepared in water, optionally mixed with a nontoxic surfactant. Dispersions can also be prepared in glycerol, liquid polyethylene 30 glycols, triacetin, and mixtures thereof and in oils. Under ordinary conditions of storage and use, these preparations contain a preservative to prevent the growth of microorganisms.

Pharmaceutical dosage forms suitable for injection or infusion can include sterile aqueous solutions or dispersions or sterile powders comprising the active ingredient which

are adapted for the extemporaneous preparation of sterile injectable or infusible solutions or dispersions, optionally encapsulated in liposomes. In all cases, the ultimate dosage form should be sterile, fluid and stable under the conditions of manufacture and storage. The liquid carrier or vehicle can be a solvent or liquid dispersion medium comprising, for 5 example, water, ethanol, a polyol (for example, glycerol, propylene glycol, liquid polyethylene glycols, and the like), vegetable oils, nontoxic glyceryl esters, and suitable mixtures thereof. The proper fluidity can be maintained, for example, by the formation of liposomes, by the maintenance of the required particle size in the case of dispersions or by the use of surfactants. The prevention of the action of microorganisms can be brought 10 about by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, sorbic acid, thimerosal, and the like. In many cases, it will be preferable to include isotonic agents, for example, sugars, buffers or sodium chloride. Prolonged absorption of the injectable compositions can be brought about by the use in the compositions of agents delaying absorption, for example, aluminum monostearate and gelatin.

15 Sterile injectable solutions can be prepared by incorporating the active compound in the required amount in the appropriate solvent with various of the other ingredients enumerated above, as required, followed by filter sterilization. In the case of sterile powders for the preparation of sterile injectable solutions, the preferred methods of preparation are vacuum drying and the freeze drying techniques, which yield a powder of 20 the active ingredient plus any additional desired ingredient present in the previously sterile-filtered solutions.

For topical administration, the present compounds may be applied in pure form, i.e., when they are liquids. However, it will generally be desirable to administer them to the skin as compositions or formulations, in combination with a dermatologically acceptable 25 carrier, which may be a solid or a liquid.

Useful solid carriers include finely divided solids such as talc, clay, microcrystalline cellulose, silica, alumina and the like. Useful liquid carriers include water, alcohols or glycols or water-alcohol/glycol blends, in which the present compounds can be dissolved or dispersed at effective levels, optionally with the aid of non-toxic surfactants. Adjuvants 30 such as fragrances and additional antimicrobial agents can be added to optimize the properties for a given use. The resultant liquid compositions can be applied from absorbent pads, used to impregnate bandages and other dressings, or sprayed onto the affected area using pump-type or aerosol sprayers. Thickeners such as synthetic polymers, fatty acids,

fatty acid salts and esters, fatty alcohols, modified celluloses or modified mineral materials can also be employed with liquid carriers to form spreadable pastes, gels, ointments, soaps, and the like, for application directly to the skin of the user.

Examples of useful dermatological compositions which can be used to deliver the 5 compounds of formula I to the skin are known to the art; for example, see Jacquet et al. (U.S. Pat. No. 4,608,392), Geria (U.S. Pat. No. 4,992,478), Smith et al. (U.S. Pat. No. 4,559,157) and Wortzman (U.S. Pat. No. 4,820,508).

Useful dosages of the compounds of formula I can be determined by comparing 10 their *in vitro* activity, and *in vivo* activity in animal models. Methods for the extrapolation of effective dosages in mice, and other animals, to humans are known to the art; for example, see U.S. Pat. No. 4,938,949.

The compound is conveniently administered in unit dosage form; for example, containing 5 to 1000 mg, conveniently 10 to 750 mg, most conveniently, 50 to 500 mg of 15 active ingredient per unit dosage form. The desired dose may conveniently be presented in a single dose or as divided doses administered at appropriate intervals, for example, as two, three, four or more sub-doses per day. The sub-dose itself may be further divided, e.g., into a number of discrete loosely spaced administrations; such as multiple inhalations from an insufflator or by application of a plurality of drops into the eye.

For internal infections, the compositions can be administered orally or parenterally 20 at dose levels, calculated as the free base, of about 0.1 to 300 mg/kg, preferably 1.0 to 30 mg/kg of mammal body weight, and can be used in man in a unit dosage form, administered one to four times daily in the amount of 1 to 1000 mg per unit dose.

For parenteral administration or for administration as drops, as for eye infections, the compounds are presented in aqueous solution in a concentration of from about 0.1 to 25 about 10%, more preferably about 0.1 to about 7%. The solution may contain other ingredients, such as emulsifiers, antioxidants or buffers.

Generally, the concentration of the compound(s) of formula I in a liquid 30 composition, such as a lotion, will be from about 0.1-25 wt-%, preferably from about 0.5-10 wt-%. The concentration in a semi-solid or solid composition such as a gel or a powder will be about 0.1-5 wt-%, preferably about 0.5-2.5 wt-%.

The exact regimen for administration of the compounds and compositions disclosed herein will necessarily be dependent upon the needs of the individual subject being treated, the type of treatment and, of course, the judgment of the attending practitioner.

The antiviral activity of a compound of the invention can be determined using pharmacological models which are well known to the art, or using Test A described below.

The compounds of formula (I) and pharmaceutically acceptable salts thereof are useful as antiviral agents. Thus, they are useful to combat viral infections in animals, 5 including man. The compounds are generally active against herpes viruses, and are particularly useful against the varicella zoster virus, the Epstein-Barr virus, the herpes simplex virus, the human herpes virus type 8 (HHV-8) and the cytomegalovirus (CMV).

CLAIMS

We claim:

1. A method of selecting compounds that inhibit herpes viruses comprising:
 - a) measuring IC₅₀ of a compound of interest that inhibits a wild type herpes virus,
 - 5 b) measuring IC₅₀ of the same compound that inhibits a binding domain mutant herpes virus which is the same strain as the wild type herpes virus,
 - c) comparing IC₅₀ of step a with IC₅₀ of step b; and
 - d) selecting the compound of interest wherein the IC₅₀ of step b is at least 3 times greater than the IC₅₀ of step a.
- 10
2. A method of selecting compounds that inhibit herpes viruses comprising:
 - a) measuring IC₅₀ of a compound of interest that inhibits a binding domain mutant herpes virus,
 - b) measuring IC₅₀ of the same compound that inhibits a wild type herpes virus which is
 - 15 the same strain as the mutant herpes virus,
 - c) comparing IC₅₀ of step a with IC₅₀ of step b; and
 - d) selecting the compound of interest wherein the IC₅₀ of step a is at least 3 times greater than the IC₅₀ of step b.
- 20
3. The method of claim 1 or 2 wherein the herpes virus is HSV-1, HSV-2, HCMV, VZV, EBV, or HHV-8.
4. A method of selecting compounds that inhibit herpes viruses comprising:
 - a) measuring IC₅₀ of a compound of interest that inhibits a wild type HSV-1,
 - 25 b) measuring IC₅₀ of the same compound that inhibits a binding domain mutant HSV-1 which is the same strain as the wild type herpes virus,
 - c) comparing IC₅₀ of step a with IC₅₀ of step b; and
 - d) selecting the compound of interest wherein the IC₅₀ of step b is at least 3 times greater than the IC₅₀ of step a.
- 30
5. A method of selecting compounds that inhibit herpes viruses comprising:
 - a) measuring IC₅₀ of a compound of interest that inhibits a binding domain mutant HSV-1,

- b) measuring IC_{50} of the same compound that inhibits a wild type herpes virus which is the same strain as the mutant HSV-1,
- c) comparing IC_{50} of step a with IC_{50} of step b; and
- d) selecting the compound of interest wherein the IC_{50} of step a is at least 3 times greater than the IC_{50} of step b.

5

- 6. The method of claim 4 or 5 wherein HSV-1 is HSV-1 KOS, HSV-1 F, HSV-1 DJL or HSV-1 Patton.

10

- 7. The method of claim 5 or 6 wherein the mutation of a wild type herpes virus to mutant herpes virus is at amino acid 823 from valine to alanine.

15

- 8. A method of selecting compounds that inhibit herpes viruses comprising:
 - a) measuring IC_{50} of a compound of interest that inhibits a wild type HSV-2,
 - b) measuring IC_{50} of the same compound that inhibits a binding domain mutant HSV-2 which is the same strain as the wild type herpes virus,
 - c) comparing IC_{50} of step a with IC_{50} of step b; and
 - d) selecting the compound of interest wherein the IC_{50} of step b is at least 3 times greater than the IC_{50} of step a.

20

- 9. A method of selecting compounds that inhibit herpes viruses comprising:
 - a) measuring IC_{50} of a compound of interest that inhibits a binding domain mutant HSV-2,
 - b) measuring IC_{50} of the same compound that inhibits a wild type herpes virus which is the same strain as the mutant HSV-2,
 - c) comparing IC_{50} of step a with IC_{50} of step b; and
 - d) selecting the compound of interest wherein the IC_{50} of step a is at least 3 times greater than the IC_{50} of step b.

25

- 10. The method of claim 8 or 9 wherein HSV-2 is HSV-2 MS, HSV-2 35D, or HSV-2 186.

30

- 11. A method of selecting compounds that inhibit herpes viruses comprising:

- a) measuring IC_{50} of a compound of interest that inhibits a wild type HCMV,
- b) measuring IC_{50} of the same compound that inhibits a binding domain mutant HCMV which is the same strain as the wild type herpes virus,
- c) comparing IC_{50} of step a with IC_{50} of step b; and
- 5 d) selecting the compound of interest wherein the IC_{50} of step b is at least 3 times greater than the IC_{50} of step a.

12. A method of selecting compounds that inhibit herpes viruses comprising:

- a) measuring IC_{50} of a compound of interest that inhibits a binding domain mutant HCMV,
- 10 b) measuring IC_{50} of the same compound that inhibits a wild type herpes virus which is the same strain of the mutant HCMV,
- c) comparing IC_{50} of step a with IC_{50} of step b; and
- 15 d) selecting the compound of interest wherein the IC_{50} of step a is at least 3 times greater than the IC_{50} of step b.

13. The method of claim 8 or 9 wherein HCMV is AD169.

14. The methods of claims 1, 4, 8, or 11 wherein IC_{50} of step b is at least 5 times greater than the IC_{50} of step a.

20

15. The methods of claims 2, 5, 9, or 12 wherein IC_{50} of step a is at least 5 times greater than the IC_{50} of step b.

25

16. A use of compounds for manufacturing of medicinals for selectively treating diseases caused by herpes viruses in a human host comprising administering a compound to a human in need of such treatment wherein said compound inhibits herpes viruses by interaction with the binding domain in the viral DNA polymerase.

30

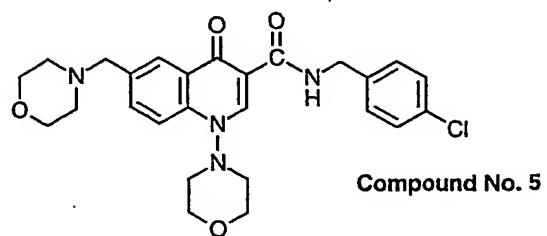
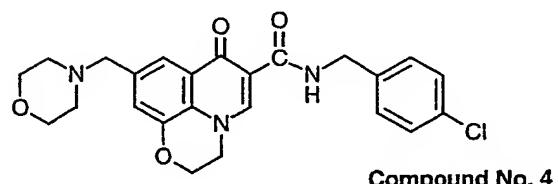
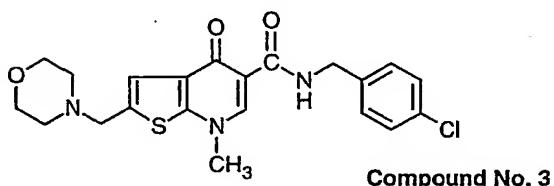
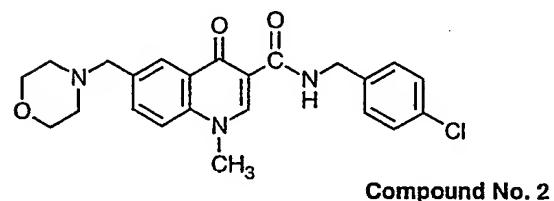
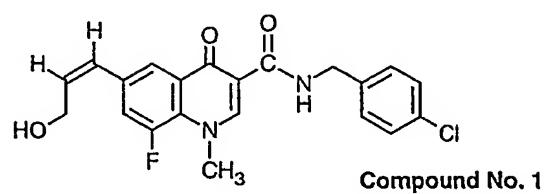
17. A use of compounds for manufacturing of medicinals for selectively inhibiting herpes viruses in a human host comprising administering a compound to a human in need of such treatment wherein IC_{50} of the compound that inhibits a binding domain

mutant herpes virus is at lease 3 times greater than IC₅₀ of the compound that inhibits a wild type herpes virus which is the same strain as the mutant herpes virus.

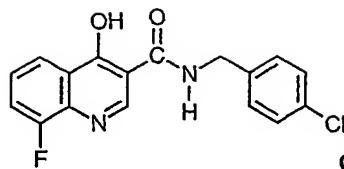
18. The use of claim 17 wherein IC₅₀ of the compound that inhibits a binding domain mutant herpes virus is at lease 5 times greater than IC₅₀ of the compound that inhibits a wild type herpes virus which is the same strain as the mutant herpes virus.
19. The use of claim 17 wherein herpes viruses is HSV-1, HSV-2, HCMV, VZV, EBV, or HHV-8.
20. A use of compounds for manufacturing of medicinals for treating herpesviral infections in a human host wherein IC₅₀ of the compound that inhibits a binding domain mutant herpes virus is at lease 5 times greater than IC₅₀ of the compound that inhibits a wild type herpes virus which is the same strain as the mutant herpes virus.
21. A use of compounds for manufacturing of medicinals for treating herpesviral infections in a human host wherein said compound inhibits the herpesvirus by interacting with the binding domain in the viral DNA polymerase.
22. The herpesviral infection of claim 20 or 21 which is HSV-1, HSV-2, HCMV, VZV, EBV, or HHV-8 infection.
23. A compound for the inhibiting of herpesvirus DNA polymerases wherein passage of a wild type herpes virus in the presence of said compound results a change of the wild type HSV-1 polymerases at amino acid 823 from valine to alanine.
24. A compound for inhibiting herpesvirus DNA polymerases wherein passage of a wild type herpes virus in the presence of said compound results in a change of the wild type HCMV polymerases at amino acid 823 from valine to alanine and at amino acid 824 from valine to leuline.

25. A mutant herpesvirus DNA molecule having a nucleotide sequence selected from a group consisting of SEQ.ID.NO. 1; SEQ.ID.NO. 3; SEQ.ID.NO. 5; SEQ.ID.NO. 7; SEQ.ID.NO. 9; and SEQ.ID.NO. 11.
- 5 26. A mutant herpesvirus polymerase amino acid molecule having an amino acid sequence selected from a group consisting of SEQ.ID.NO. 2; SEQ.ID.NO. 4; SEQ.ID.NO. 6; SEQ.ID.NO. 8; SEQ.ID.NO. 10 and SEQ.ID.NO. 12.

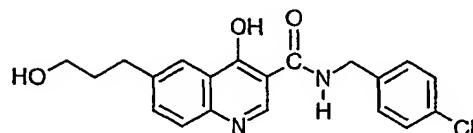
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Figure 1 4-HQ, 4-oxo-DHQ and 4-oxo-DHTP antiviral compounds

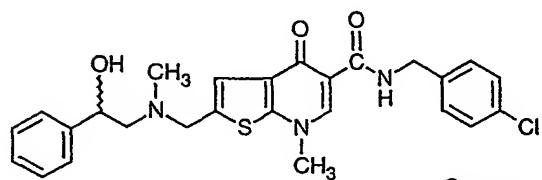
(Figure 1 continue)



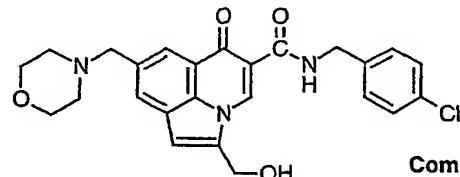
Compound No. 6



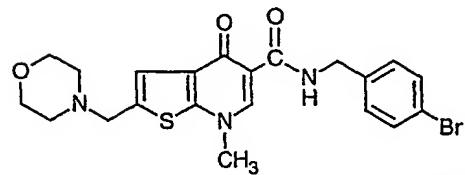
Compound No. 7



Compound No. 8

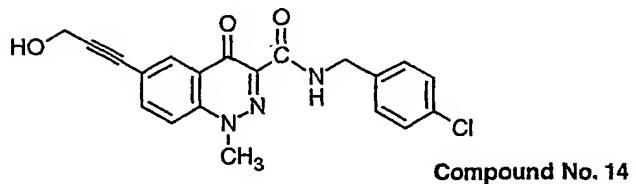
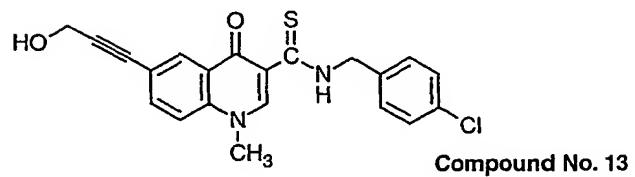
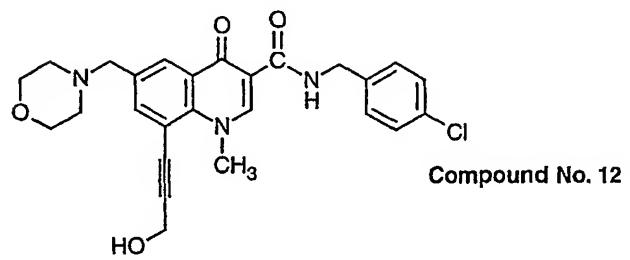
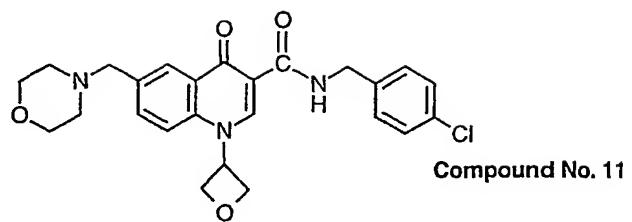


Compound No. 9

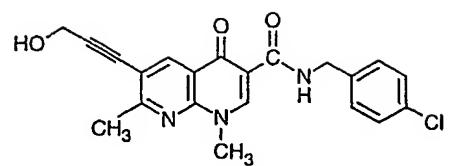


Compound No. 10

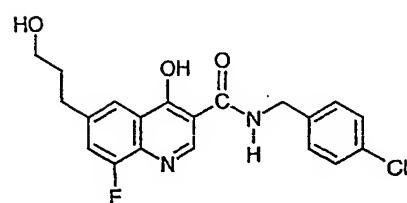
(Figure 1 continue)



(Figure 1 continue)

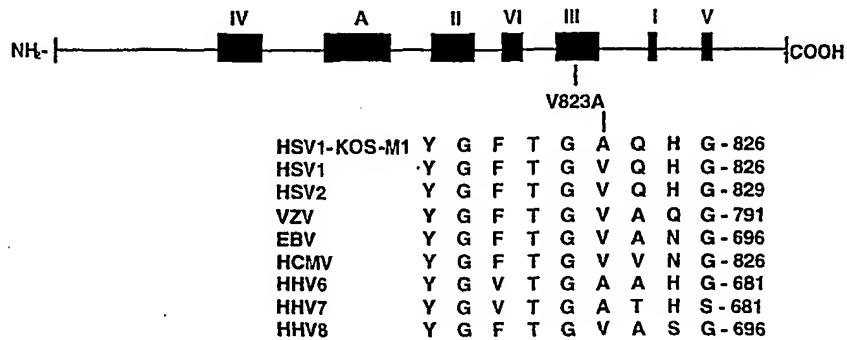


Compound No.15



Compound 17

Figure 2. The HSV1 (KOS Strain) DNA Polymerase Amino Acid 823 is Critical for Resistance to 4-Hydroxyquinolines and Related Compounds



Schematic of HSV1 polymerase illustrating the conserved regions A and I-VI found in class 2 polymerases. Also shown are the amino acid sequence for the highly conserved herpesvirus domain in region III which surrounds the HSV1 amino acid 823.

Figure 3 Serial Passage of HSV-1 in Presence of 20 μ M compound 17

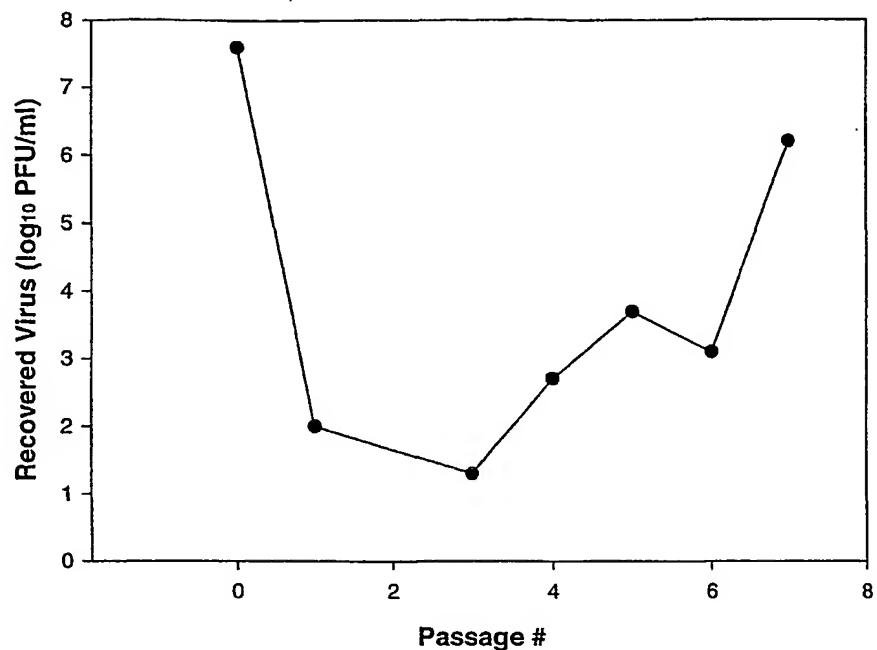


Figure 4 Comparison of Wild type HSV-1 and HSV-2 DNA Polymerases Amino Acid Sequences Aligned by Amino Acid Homology*

	HSV2-MS	MFCAAGGPTS PGGKSAARAA SGFFAPHNPR GATQTAPPPC RRQNFYNPHL -50
	HSV2-186	MFCAAGGPAS PGGKSAARAA SGFFAPHNPR GATQTAPPPC RRQNFYNPHL -50
5	HSV1-Kos	MFSGGGGPLS PGGKSAARAA SGFFAPAGPR GAGR.GPPPC LRQNFYNPYL -49
	HSV1-Patton	MFSGGGGPLS PGGKSAARAA SGFFAPAGPR GAGR.GPPPC LRQNFYNPYL -49
	HSV1-DJL	MFSGGGGPLS PGGKSAARAA SGFFAPAGPR GAGR.GPPPC LRQNFYNPYL -49
	HSV1-F	MFSGGGGPLS PGGKSAARAA SGFFAPAGPR GAGR.GPPPC LRQNFYNPYL -49
10	HSV2-MS	AQTGTQPKAP GPAQRHTYY S ECDEFRFIA P RSLDEDAPAE QRTGVHDGRL -100
	HSV2-186	AQTGTQPKAP GPAQRHTYY S ECDEFRFIA P RSLDEDAPAE QRTGVHDGRL -100
	HSV1-Kos	APVGTQQKPT GPTQRHTYY S ECDEFRFIA P RVLDEDAPPE KRAVGHDGHL -99
	HSV1-Patton	APVGTQQKPT GPTQRHTYY S ECDEFRFIA P RVLDEDAPPE KRAVGHDGHL -99
15	HSV1-DJL	APVGTQQKPT GPTQRHTYY S ECDEFRFIA P RVLDEDAPPE KRAVGHDGHL -99
	HSV1-F	APVGTQQKPT GPTQRHTYY S ECDEFRFIA P RVLDEDAPPE KRAVGHDGHL -99
	HSV2-MS	RRAPKVYCGG DERDVLRVGP EGFWPRLRL WGGADHAPKG FDPTVTVFHV -150
	HSV2-186	RRAPKVYCGG DERDVLRVGP EGFWPRLRL WGGADHAPEG FDPTVTVFHV -150
	HSV-Kos	KRAPKVYCGG DERDVLRVGS GGFWPRLRL WGGVDHAPAG FNPTVTVFHV -149
20	HSV1-Patton	KRAPKVYCGG DERDVLRVGS GGFWPRLRL WGGVDHAPAG FNPTVTVFHV -149
	HSV1-DJL	KRAPKVYCGG DERDVLRVGS GGFWPRLRL WGGVDHAPAG FNPTVTVFHV -149
	HSV1-F	KRAPKVYCGG DERDVLRVGS GGFWPRLRL WGGVDHAPAG FNPTVTVFHV -149
25	HSV2-MS	YDILEHVEHA YSMRAAQLHE RFMDAITPAG TVITLLGLTP EGHRAVHVY -200
	HSV2-186	YDILEHVEHA YSMRAAQLHE RFMDAITPAG TVITLLGLTP EGHRAVHVY -200
	HSV-Kos	YDILENVEHA YGMRAAQFHA RFMDAITPTG TVITLLGLTP EGHRAVHVY -199
	HSV1-Patton	YDILENVEHA YGMRAAQFHA RFMDAITPTG TVITLLGLTP EGHRAVHVY -199
	HSV1-DJL	YDILENVEHA YGMRAAQFHA RFMDAITPTG TVITLLGLTP EGHRAVHVY -199
	HSV1-F	YDILENVEHA YGMRAAQFHA RFMDAITPTG TVITLLGLTP EGHRAVHVY -199
30	HSV2-MS	GTRQYFYMNK AEVDRHLQCR APRDLCERLA AALRESPGAS FRGISADHFE -250
	HSV2-186	GTRQYFYMNK AEVDRHLQCR APRDLCERLA AALRESPGAS FRGISADHFE -250
	HSV-Kos	GTRQYFYMNK EEVDRHLQCR APRDLCERLA AALRESPGAS FRGISADHFE -249
	HSV1-Patton	GTRQYFYMNK EEVDRHLQCR APRDLCERLA AALRESPGAS FRGISADHFE -249
35	HSV1-DJL	GTRQYFYMNK EEVDRHLQCR APRDLCERLA AALRESPGAS FRGISADHFE -249
	HSV1-F	GTRQYFYMNK EEVDRHLQCR APRDLCERLA AALRESPGAS FRGISADHFE -249
	HSV2-MS	AEVVERADV Y YETRPTL YY RVFVRSGRAL AYLCDNFCPA IRKYEGGVDA -300
	HSV2-186	AEVVERADV Y YETRPTL YY RVFVRSGRAL AYLCDNFCPA IRKYEGGVDA -300
40	HSV-Kos	AEVVERTDV Y YETRPA LFY RVYVRSGRVL SYLCDNFCPA IKKYEGGVDA -299
	HSV1-Patton	AEVVERTDV Y YETRPA LFY RVYVRSGRVL SYLCDNFCPA IKKYEGGVDA -299
	HSV1-DJL	AEVVERTDV Y YETRPA LFY RVYVRSGRVL SYLCDNFCPA IKKYEGGVDA -299
	HSV1-F	AEVVERTDV Y YETRPA LFY RVYVRSGRVL SYLCDNFCPA IKKYEGGVDA -299
45	HSV2-MS	TTRFI LDNPG FVTFGWYRLK PGRGNAPAQP RPPTA FGTSS DVEFNCTADN -350
	HSV2-186	TTRFI LDNPG FVTFGWYRLK PGRGNAPAQP RPPTA FGTSS DVEFNCTADN -350
	HSV-Kos	TTRFI LDNPG FVTFGWYRLK PGRNN TLAQP RAPMA FGTSS DVEFNCTADN -349
	HSV1-Patton	TTRFI LDNPG FVTFGWYRLK PGRNN TLAQP RAPMA FGTSS DVEFNCTADN -349
50	HSV1-DJL	TTRFI LDNPG FVTFGWYRLK PGRNN TLAQP RAPMA FGTSS DVEFNCTADN -349
	HSV1-F	TTRFI LDNPG FVTFGWYRLK PGRNN TLAQP RAPMA FGTSS DVEFNCTADN -349
	HSV2-MS	LAVEGAMCDL PAYKLMCFDI ECKAGGEDEL AFPVAERPED LVIQISCLLY -400
	HSV2-186	LAVEGAMCDL PAYKLMCFDI ECKAGGEDEL AFPVAERPED LVIQISCLLY -400
	HSV-Kos	LAIEGGMSDL PAYKLMCFDI ECKAGGEDEL AFPVAGHPED LVIQISCLLY -399
55	HSV1-Patton	LAIEGGMSDL PAYKLMCFDI ECKAGGEDEL AFPVAGHPED LVIQISCLLY -399
	HSV1-DJL	LAIEGGMSDL PAYKLMCFDI ECKAGGEDEL AFPVAGHPED LVIQISCLLY -399
	HSV1-F	LAIEGGMSDL PAYKLMCFDI ECKAGGEDEL AFPVAGHPED LVIQISCLLY -399
	HSV2-MS	DLSTTALEHI LLFSLGSCDL PESHLSDLAS RGLPAPVVL FDSEFEMLLA -450
60	HSV2-186	DLSTTALEHI LLFSLGSCDL PESHLSDLAS RGLPAPVVL FDSEFEMLLA -450
	HSV-Kos	DLSTTALEHV LLFSLGSCDL PESHLNELAA RGLPTPVVL FDSEFEMLLA -449
	HSV1-Patton	DLSTTALEHV LLFSLGSCDL PESHLNELAA RGLPTPVVL FDSEFEMLLA -449
	HSV1-DJL	DLSTTALEHV LLFSLGSCDL PESHLNELAA RGLPTPVVL FDSEFEMLLA -449
65	HSV1-F	DLSTTALEHV LLFSLGSCDL PESHLNELAA RGLPTPVVL FDSEFEMLLA -449

	HSV2-MS	FMTFKQYGP	EFVTGYNIIN	FDWPFLTLKL	TEIYKVPLDG	YGRMNGRGVF	-500
	HSV2-186	FMTFKQYGP	EFVTGYNIIN	FDWPFLTLKL	TEIYKVPLDG	YGRMNGRGVF	-500
	HSV-Kos	FMTLVKQYGP	EFVTGYNIIN	FDWPFLLAKL	TDIYKVPLDG	YGRMNGRGVF	-499
	HSV1-Patton	FMTLVKQYGP	EFVTGYNIIN	FDWPFLLAKL	TDIYKVPLDG	YGRMNGRGVF	-499
5	HSV1-DJL	FMTLVKQYGP	EFVTGYNIIN	FDWPFLLAKL	TDIYKVPLDG	YGRMNGRGVF	-499
	HSV1-F	FMTLVKQYGP	EFVTGYNIIN	FDWPFLLAKL	TDIYKVPLDG	YGRMNGRGVF	-499
	HSV2-MS	RVWDIGQSHF	QKRSKIKVNG	MVNIDMYGII	TDKVLSSYK	LNAVAEAVLK	-550
	HSV2-186	RVWDIGQSHF	QKRSKIKVNG	MVNIDMYGII	TDKVLSSYK	LNAVAEAVLK	-550
10	HSV-Kos	RVWDIGQSHF	QKRSKIKVNG	MVNIDMYGII	TDKIKLSSYK	LNAVAEAVLK	-549
	HSV1-Patton	RVWDIGQSHF	QKRSKIKVNG	MVNIDMYGII	TDKIKLSSYK	LNAVAEAVLK	-549
	HSV1-DJL	RVWDIGQSHF	QKRSKIKVNG	MVNIDMYGII	TDKIKLSSYK	LNAVAEAVLK	-549
	HSV1-F	RVWDIGQSHF	QKRSKIKVNG	MVNIDMYGII	TDKIKLSSYK	LNAVAEAVLK	-549
15	HSV2-MS	DKKKDLSYRD	IPAYYASGPA	QRGVIGEYCV	QDSLLVGQLF	FKFLPHLELS	-600
	HSV2-186	DKKKDLSYRD	IPAYYASGPA	QRGVIGEYCV	QDSLLVGQLF	FKFLPHLELS	-600
	HSV-Kos	DKKKDLSYRD	IPAYYAAGPA	QRGVIGEYCI	QDSLLVGQLF	FKFLPHLELS	-599
	HSV1-Patton	DKKKDLSYRD	IPAYYAAGPA	QRGVIGEYCI	QDSLLVGQLF	FKFLPHLELS	-599
20	HSV1-DJL	DKKKDLSYRD	IPTYYAAGPA	QRGVIGEYCI	QDSLLVGQLF	FKFLPHLELS	-599
	HSV1-F	DKKKDLSYRD	IPAYYAAGPA	QRGVIGEYCI	QDSLLVGQLF	FKFLPHLELS	-599
	HSV2-MS	AVARLAGINI	TRTIYDGQQI	RVFTCLRLA	GQKGFLPDT	QGRFRGLDKE	-650
	HSV2-186	AVARLAGINI	TRTIYDGQQI	RVFTCLRLA	GQKGFLPDT	QGRFRGLDKE	-650
	HSV-Kos	AVARLAGINI	TRTIYDGQQI	RVFTCLRLA	DQKGFLPDT	QGRFRGAGGE	-649
25	HSV1-Patton	AVARLAGINI	TRTIYDGQQI	RVFTCLRLA	DQKGFLPDT	QGRFRGAGGE	-649
	HSV1-DJL	AVARLAGINI	TRTIYDGQQI	RVFTCLRLA	DQKGFLPDT	QGRFRGAGGE	-649
	HSV1-F	AVARLAGINI	TRTIYDGQQI	RVFTCLRLA	DQKGFLPDT	QGRFRGAGGE	-649
	HSV2-MS	APKRPAVPRG	EGERPGDGNG	DEDKDDDE..	DEDGDERE.E	VARETGRHV	-697
30	HSV2-186	APKRPAVPRG	EGERPGDGNG	DEDKDDDEDG	DEDGDERE.E	VARETGRHV	-697
	HSV-Kos	APKRPAARE	DEERP.....	EEEGEDEDER	EEGGGEREPE	GARETAGRHV	-694
	HSV1-Patton	APKRPAARE	DEERP.....	EEEGEDEDER	EEGGGEREPE	GARETAGRHV	-694
	HSV1-DJL	APKRPAARE	DEERP.....	EEEGEDENER	EEGGGEREPE	GARETAGRHV	-694
	HSV1-F	APKRPAARE	DEERP.....	EEEGEDEDER	EEGGGEREPE	GARETAGRHV	-694
35	HSV2-MS	GYQGARVLDP	TSGFHVDPPV	VFDFASLYPS	IIQAHNLCFS	TLSLRPEAVA	-747
	HSV2-186	GYQGARVLDP	TSGFHVDPPV	VFDFASLYPS	IIQAHNLCFS	TLSLRPEAVA	-749
	HSV-Kos	GYQGARVLDP	TSGFHVNPPV	VFDFASLYPS	IIQAHNLCFS	TLSLRADAVA	-744
	HSV1-Patton	GYQGARVLDP	ISGFHVNPPV	VFDFASLYPS	IIQAHNLCFS	TLSLRADAVA	-744
40	HSV1-DJL	GYQGARVLDP	TSGFHVNPPV	VFDFASLYPS	IIQAHNLCFS	TLSLRADAVA	-744
	HSV1-F	GYQGARVLDP	TSGFHVNPPV	VFDFASLYPS	IIQAHNLCFS	TLSLRADAVA	-744
	HSV2-MS	HLEADRDL	IEVGGRRLFF	VKAHVRESLL	SILLRDWLAM	RKQIRSRIPQ	-797
	HSV2-186	HLEADRDL	IEVGGRRLFF	VKAHVRESLL	SILLRDWLAM	RKQIRSRIPQ	-799
45	HSV-Kos	HLEAGKD	IEVGGRRLFF	VKAHVRESLL	SILLRDWLAM	RKQIRSRIPQ	-794
	HSV1-Patton	HLEAGKD	IEVGGRRLFF	VKAHVRESLL	SILLRDWLAM	RKQIRSRIPQ	-794
	HSV1-DJL	HLEAGKD	IEVGGRRLFF	VKAHVRESLL	SILLRDWLAM	RKQIRSRIPQ	-794
	HSV1-F	HLEAGKD	IEVGGRRLFF	VKAHVRESLL	SILLRDWLAM	RKQIRSRIPQ	-794
50	HSV2-MS	STPEEAVLLD	KQQAAIKVVC	NSVYGFVGQ	HGLLPCLHVA	ATVTTIGREM	-847
	HSV2-186	SPPEEAVLLD	KQQAAIKVVC	NSVYGFVGQ	HGLLPCLHVA	ATVTTIGREM	-849
	HSV-Kos	SSPEEAVLLD	KQQAAIKVVC	NSVYGFVGQ	HGLLPCLHVA	ATVTTIGREM	-844
	HSV1-Patton	SSPEEAVLLD	KQQAAIKVVC	NSVYGFVGQ	HGLLPCLHVA	ATVTTIGREM	-844
	HSV1-DJL	SSPEEAVLLD	KQQAAIKVVC	NSVYGFVGQ	HGLLPCLHVA	ATVTTIGREM	-844
55	HSV1-F	SSPEEAVLLD	KQQAAIKVVC	NSVYGFVGQ	HGLLPCLHVA	ATVTTIGREM	-844
	HSV2-MS	LLATRAYVHA	RWAEFDQLLA	DFPEAAGMRA	PGPYSMRIIY	GDTDSIFVLC	-897
	HSV2-186	LLATRAYVHA	RWAEFDQLLA	DFPEAAGMRA	PGPYSMRIIY	GDTDSIFVLC	-899
	HSV-Kos	LLATREYVHA	RWAAFEQLLA	DFPEAADMRA	PGPYSMRIIY	GDTDSIFVLC	-894
60	HSV1-Patton	LLATREYVHA	RWAAFEQLLA	DFPEAADMRA	PGPYSMRIIY	GDTDSIFVLC	-894
	HSV1-DJL	LLATREYVHA	RWAAFEQLLA	DFPEAADMRA	PGPYSMRIIY	GDTDSIFVLC	-894
	HSV1-F	LLATREYVHA	RWAAFEQLLA	DFPEAADMRA	PGPYSMRIIY	GDTDSIFVLC	-894
	HSV2-MS	RGLTAAGLVA	MGDKMASHIS	RALFLPPIKL	ECEKTFKLL	LIAKKKYIGV	-947
	HSV2-186	RGLTAAGLVA	MGDKMASHIS	RALFLPPIKL	ECEKTFKLL	LIAKKKYIGV	-949
	HSV-Kos	RGLTAAGLTA	MGDKMASHIS	RALFLPPIKL	ECEKTFKLL	LIAKKKYIGV	-944
65	HSV1-Patton	RGLTAAGLTA	MGDKMASHIS	RALFLPPIKL	ECEKTFKLL	LIAKKKYIGV	-944

	HSV1-DJL	RGLTAAGLTA VGDKMASHIS RALFLPPIKL ECEKTFKLL LIAKKYIGV -944
	HSV1-F	RGLTAAGLTA VGDKMASHIS RALFLPPIKL ECEKTFKLL LIAKKYIGV -944
5	HSV2-MS	IYGGKMLIKG VDLVRKNNCA FINRTSRALV DLLFYDDTVS GAAAALAERP -997
	HSV2-186	IYGGKMLIKG VDLVRKNNCA FINRTSRALV DLLFYDDTVS GAAAALAERP -999
	HSV-Kos	IYGGKMLIKG VDLVRKNNCA FINRTSRALV DLLFYDDTVS GAAAALAERP -994
	HSV1-Patton	IYGGKMLIKG VDLVRKNNCA FINRTSRALV DLLFYDDTVS GAAAALAERP -994
	HSV1-DJL	IYGGKMLIKG VDLVRKNNCA FINRTSRALV DLLFYDDTVS GAAAALAERP -994
10	HSV1-F	IYGGKMLIKG VDLVRKNNCA FINRTSRALV DLLFYDDTVS GAAAALAERP -994
	HSV2-MS	AEEWLARPLP EGLQAFGAVL VDAHRRITDP ERDIQDFVLT AELSRHPRAY -1047
	HSV2-186	AEEWLARPLP EGLQAFGAVL VDAHRRITDP ERDIQDFVLT AELSRHPRAY -1049
	HSV-Kos	AEEWLARPLP EGLQAFGAVL VDAHRRITDP ERDIQDFVLT AELSRHPRAY -1044
	HSV1-Patton	AEEWLARPLP EGLQAFGAVL VDAHRRITDP ERDIQDFVLT AELSRHPRAY -1044
15	HSV1-DJL	AEEWLARPLP EGLQAFGAVL VDAHRRITDP ERDIQDFVLT AELSRHPRAY -1044
	HSV1-F	AEEWLARPLP EGLQAFGAVL VDAHRRITDP ERDIQDFVLT AELSRHPRAY -1044
20	HSV2-MS	TNKRLAHLTV YYKLMARRAQ VPSIKDRIPY VIVAQTREVE ETVARLAALR -1097
	HSV2-186	TNKRLAHLTV YYKLMARRAQ VPSIKDRIPY VIVAQTREVE ETVARLAALR -1099
	HSV-Kos	TNKRLAHLTV YYKLMARRAQ VPSIKDRIPY VIVAQTREVE ETVARLAALR -1094
	HSV1-Patton	TNKRLAHLTV YYKLMARRAQ VPSIKDRIPY VIVAQTREVE ETVARLAALR -1094
	HSV1-DJL	TNKRLAHLTV YYKLMARRAQ VPSIKDRIPY VIVAQTREVE ETVARLAALR -1094
	HSV1-F	TNKRLAHLTV YYKLMARRAQ VPSIKDRIPY VIVAQTREVE ETVARLAALR -1094
25	HSV2-MS	ELDAAAAPGDE PAPPAALPSP AKRPRETPSH ADPPGGASKP RKLLVSELAE -1147
	HSV2-186	ELDAAAAPGDE PAPPAALPSP AKRPRETPSH ADPPGGASKP RKLLVSELAE -1149
	HSV-Kos	ELDAAAAPGDE PAPPAALPSP AKRPRETPSH ADPPGGASKP RKLLVSELAE -1144
	HSV1-Patton	ELDAAAAPGDE PAPPAALPSP AKRPRETPSP ADPPGGASKP RKLLVSELAE -1144
30	HSV1-DJL	ELDAAAAPGDE PAPPAALPSP AKRPRETPSP ADPPGGASKP RKLLVSELAE -1144
	HSV1-F	ELDAAAAPGDE PAPPAALPSP AKRPRETPSH ADPPGGASKP RKLLVSELAE -1144
35	HSV2-MS	DPGYAIARGV PLNTDYYFSH LLGAAACVTFK ALFGNNAKIT ESLLKRFIPE -1197
	HSV2-186	DPGYAIARGV PLNTDYYFSH LLGAAACVTFK ALFGNNAKIT ESLLKRFIPE -1199
	HSV-Kos	DPAYAIAHGV ALNTDYYFSH LLGAAACVTFK ALFGNNAKIT ESLLKRFIPE -1194
	HSV1-Patton	DPAYAIAHGV ALNTDYYFSH LLGAAACVTFK ALFGNNAKIT ESLLKRFIPE -1194
	HSV1-DJL	DPAYAIAHGV ALNTDYYFSH LLGAAACVTFK ALFGNNAKIT ESLLKRFIPE -1194
	HSV1-F	DPAYAIAHGV ALNTDYYFSH LLGAAACVTFK ALFGNNAKIT ESLLKRFIPE -1194
40	HSV2-MS	TWHPDDVA A RLRAAGFGPA GAGATAEETR RMLHRAFDTL A* -1238
	HSV2-186	TWHPDDVA A RLRAAGFGPA GAGATAEETR RMLHRAFDTL A* -1240
	HSV-Kos	VWHPDDVA A RLRAAGFGAV GAGATAEETR RMLHRAFDTL A* -1235
	HSV1-Patton	VWHPDDVTA RLRAAGFGAV GAGATAEETR RMLHRAFDTL A* -1235
	HSV1-DJL	VWHPDDVA A RLRTAGFGAV GAGATAEETR RMLHRAFDTL A* -1235
	HSV1-F	VWHPDDVA A RLRAAGFGAV GAGATAEETR RMLHRAFDTL A* -1235
45		

*Amino acid alignment demonstrates difference in amino acid's sequences.

*The gaps “....” indicate missing amino acids relative to other stanins.

*Wild HSV2-MS is listed as SEQ. ID NO 14.

*Wild HSV2-186 is listed as SEQ. ID NO 15.

50 *Wild HSV-Kos is listed as SEQ. ID NO 16.

*Wild HSV1-Patton is listed as SEQ. ID NO 17.

*Wild HSV1-DJL is listed as SEQ. ID NO 18.

*Wild HSV1-F is listed as SEQ. ID NO 19.

Figure 5 DNA and amino acid sequence list

SEQ. ID. NO. 1 DNA sequence of DNA polymerase gene for HSV2-MS-M1

5 1 ATGTTTTGTG CCGCGGGCGG CCCGACTTCC CCCGGGGGGA AGTCGGCGGC
51 TCGGGCGGCG TCTGGGTTTT TTGCCCCCA CAACCCCCGG GGAGCCACCC
101 AGACGGCACC GCCGCCTTGC CGCCGGCAGA ACTTCTACAA CCCCCACCTC
10 151 GCTCAGACCG GAACGCAGCC AAAGGCCCCC GGGCCGGCTC AGCGCCATAC
201 GTACTACAGC GAGTGCAGC AATTTCGATT TATGCCCG CGTCGCTGG
15 251 ACGAGGACGC CCCCCGGAG CAGCGCACCG GGGTCCACGA CGGCCGCCTC
301 CGGCGCGCCC CTAAGGTGTA CTGCGGGGG GACGAGCGCG ACGTCCTCCG
351 CGTGGGCCCG GAGGGCTTCT GGCGCGTCG CTTGCCCTG TGGGGCGGTG
20 401 CGGACCATGC CCCCCAAGGGG TTCGACCCCA CCGTCACCGT CTTCCACGTG
451 TACGACATCC TGGAGCACGT GGAACACGCG TACAGCATGC GCGCCGCCA
25 501 GCTCCACGAG CGATTATGG ACCCCATCAC GCCCCGCCGG ACCGTCA
551 CGCTTCTGGG TCTGACCCCA GAAGGCCATC GCGTCGCCGT TCACGTCTAC
601 GGCACGCGGC AGTACTTTA CATGAACAAG GCGGAGGTGG ATCGGCACCT
30 651 GCAGTGCCGT GCCCCGCGCG ATCTCTGCGA GCGCCTGGCG GCGGCCCTGC
701 GCGAGTCGCC GGGGGCGTCG TTCCGCGGCA TCTCCGCGGA CCACCTCGAG
35 751 GCGGAGGTGG TGGAGCGCGC CGACGTGTAC TATTACGAAA CGCGCCCGAC
801 CCTGTACTAC CGCGTCTTCG TGCGAAGCGG GCGCGCGCTG GCCTACCTGT
851 GCGACAACCTT TTGCCCCCGCG ATCAGGAAGT ACGAGGGGGG CGTCGACGCC
40 901 ACCACCCGGT TTATCCTGGA CAACCCGGGG TTTGTACCT TCGGCTGGTA
951 CCGCCTCAAG CCCGGCCGCG GGAACCGCGCC GGCCCAACCG CGCCCCCGA
45 1001 CGCGTTCGG AACCTCGAGC GACGTGAGT TTAACGTGAC GGCAGACAAC
1051 CTGGCCGTG AGGGGCCAT GTGTGACCTG CGGCCTACA AGCTCATGTG
50 1101 CTTCGATATC GAATGCAAGG CCGGGGGGGA GGACGGAGCTG GCCTTCCGG
1151 TCGCGGAACG CCCGAAAGAC CTCGTCATCC AGATCTCCTG TCTGCTCTAC
1201 GACCTGTCCA CCACCGCCCT CGAGCACATC CTCTGTGTTT CGCTCGGATC
55 1251 CTGCGACCTC CCCGAGTCCC ACCTCAGCGA TCTCGCCTCC AGGGGCCTGC
1301 CGGCCCCCGT CGTCCTGGAG TTTGACAGCG AATTGAGAT GCTGCTGGCC

1351 TTCATGACCT TCGTCAAGCA GTACGGCCCC GAGTCGTGA CCGGGTACAA
1401 CATCATCAAC TTCGACTGGC CCTTCGTCTT GACCAAGCTG ACGGAGATCT
5 1451 ACAAGGTCCC GCTCGACGGG TACGGGCGCA TGAACGGCCG GGGTGTGTT
1501 CGCGTGTGGG ACATCGGCCA GAGCCACTTT CAGAACGCGA GCAAGATCAA
1551 GGTGAACGGG ATGGTGAACA TCGACATGTA CGGCATCATC ACCGACAAGG
10 1601 TCAAACACTCTC CAGCTACAAG CTGAACGCCG TCGCCGAGGC CGTCTTGAAG
1651 GACAAGAAGA AGGATCTGAG CTACCGCGAC ATCCCCGCT ACTACGCCTC
15 1701 CGGGCCCGCG CAGCGCGGG TGATCGCGA GTATTGTGTG CAGGACTCCG
1751 TGCTGGTCGG GCAGCTGTTTCA TTCAAGTTTC TGCCGCACCT GGAGCTTCCC
1801 GCCGTCGCGC GCCTGGCGGG CATCAACATC ACCCGCACCA TCTACGACGG
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1901 GCTTCATCCT GCCGGACACC CAGGGCGGT TTCGGGCCT CGACAAGGAG
25 1951 GCGCCCAAGC GCCCGGCCGT GCCTCGGGGG GAAGGGGAGC GGCCGGGGGA
2001 CGGGAACGGG GACGAGGATA AGGACGACGA CGAGGACGAG GACGGGGACG
2051 AGCGCGAGGA GGTCGCGCGC GAGACGGGGG GCCGGCACGT TGGGTACCAAG
30 2101 GGGGCCCGGG TCCTCGACCC CACCTCCGGG TTTCACGTCG ACCCCGTGGT
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35 2201 TGTGCTTCAG TACGCTCTCC CTGCGGCCCG AGGCCGTCGC GCACCTGGAG
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40 2301 CGTGAAGGCC CACGTACCGCG AGAGCCTGCT GAGCATCCTG CTGCGCGACT
2351 GGCTGGCCAT GCGAAAGCAG ATCCGCTCGC GGATCCCCA GAGCACCCCC
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45 2451 CAACTCGGTG TACGGGTTCA CCGGGGCCGA GCACGGTCTT CTGCCCTGCC
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50 2601 CGACTTTCCG GAGGCGGCCG GCATGCGCGC CCCCGBTCCG TACTCCATGC
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2751 GCGCGCGCTG TTCTCCCCC CGATCAAGCT CGAGTGCAGAA AAAACGTTCA
2801 CCAAGCTGCT GCTCATCGCC AAGAAAAAGT ACATCGCGT CATCTGCGGG
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2851 GGCAAGATGC TCATCAAGGG CGTGGATCTG GTGCGCAAAA ACAACTGCGC
2901 GTTTATCAAC CGCACCTCCA GGGCCCTGGT CGACCTGCTG TTTTACGACG
5 2951 ATACCGTATC CGGAGCGGCC GCCGCGTTAG CCGAGCGCCC CGCAGAGGAG
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10 3101 TTGTCCTCAC CGCCGAAC TG AGCAGACACC CGCGCGCGTA CACCAACAAG
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15 3201 GGTCCCGTCC ATCAAGGACC GGATCCCGTA CGTGATCGTG GCCCAGACCC
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20 3351 GGCCAAGGCC CCCCCGGAGA CGCCGTGCGA TGCCGACCCC CCGGGAGGCG
3401 CGTCCAAGGCC CCGCAAGCTG CTGGTGTCCG AGCTGGCGGA GGATCCCGGG
25 3451 TACGCCATCG CCCGGGGCGT TCCGCTAAC ACGGACTATT ACTTCTCGCA
3501 CCTGCTGGGG GCGGCCTGCG TGACGTTCAA GGCCCTGTT GGAAATAACG
3551 CCAAGATCAC CGAGAGTCTG TTAAAGAGGT TTATTCCGA GACGTGGCAC
30 3601 CCCCCGGACG ACGTGGCCGC GCGGCTCAGG GCCGCGGGGT TCGGGCCGGC
3651 GGGGGCCGGC GCTACGGCGG AGGAAACTCG TCGAATGTTG CATAGAGCCT
35 3701 TTGATACTCT AGCATGA

SEQ. ID. NO. 2 Amino acid sequence of DNA polymerase for HSV2-MS-M1

1 MFCAAGGPTS PGGKSAARAA SGFFAPHNPR GATQTAPPPC RRQNFYNPHL
5 51 AQTGTQPKAP GPAQRHTYYYS ECDEFRFIA P RSLDEDAPAE QRTGVHDGRL
101 101 RRAPKVYCGG DERDVLRVGP EGFWPRLRL WGGADHAPKG FDPTVTVFHV
151 151 YDILEHVEHA YSMRAAQLHE RFMDAITPAG TVITLLGLTP EGHRVAHVY
201 201 GTRQYFYMNK AEVDRHLQCR APRDLCE RL AALRESPGAS FRGISADHFE
251 251 AEVVERADVY YYETRPTLYY RVFVRSGRAL AYLCDNFCPA IRKYEGGVDA
301 301 TTRFILDNPG FVTFGWYRLK PGRGNAPAQP RPPTAFTSS DVEFNCTADN
351 351 LAVEGAMCDL PAYKLMCFDI ECKAGGEDEL AFPVAERPED LVIQISCLLY
401 401 DLSTTALEHI LLFSLGSCDL PESHLSDLAS RGLPAPVVLE FDSEFEMLLA
451 451 FMTFVKQYGP EFVTGYNIN FDWPFLVTKL TEIYKVPLDG YGRMNGRGVF
501 501 RVWDIGQSHF.QKRSKIKVNG MVNIDMYGII TDKVKLSSYK LNAVAEAVLK
551 551 DKKKDLSYRD IPAYYASGPA QRGVIGEYCV QDSLLVGQLF FKFLPHLELS
601 601 AVARLAGINI TRTIYDGQQI RVFTCLLRLA GQKGFLPDT QGRFRGLDKE
651 651 APKRPAPVRG EGERPGDGNG DEDKDDDEDE DGDREEVAR ETGGRHVGYQ
701 701 GARVLDPTSG FHVDPVVVFD FASLYPSIIQ AHNLCFSTLS LRPEAVAHLE
751 751 ADRDYLEIEV GGRRLLFFVKA HVRESLLSIL LRDWLAMRKQ IRSRIPQSTP
801 801 EEA VLLDKQQ AAIKVVCNSV YGFTGAQHGL LPCLHVAATV TTIGREMLLA
851 851 TRAYVHARWA EFDQLLADFP EAAGMRAPGP YSMRHYGDT DSIFVLCRGL
901 901 TAAGLVAMGD KMASHISRAL FLPPIKLECE KTFTKLLLIA KKKYIGVICG
951 951 GKMLIKGVDL VRKNNCAFIN RTSRALVDLL FYDDTVSGAA AALAERPAEE
1001 1001 WLARPLPEGL QAFGAVLVDA HRRITDPERD IQDFVLTAEL SRHPRAYTNK
1051 1051 RLAHLTVYYK LMARRAQVPS IKDRIPYVIV AQTREVEETV ARLAALRELD
1101 1101 AAAPGDEPAP PAALPSPAKR PRETPSHADP PGGASKPRKL LVSELAEDPG
1151 1151 YALARGVPLN TDYYFSHLLG AACVTFKALF GNNAKITESL LKRFIPETWH
1201 1201 PPDDVAARLR AAGFGPAGAG ATAEEETRRML HRAFDTLA*

SEQ.ID.NO. 3 DNA sequence of DNA polymerase gene for HSV2-186-M1

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1 ATGTTTGTG CCGCGGGCGG CCCGGCTTCC CCCGGGGGGA AGTCGGCGGC
5 51 TCGGGCGGCG TCTGGGTTTT TTGCCCCCCA CAACCCCCGG GGAGGCCACCC
10 101 AGACGGCACC GCCGCCTTGC CGCCGGCAGA ACTTCTACAA CCCCCCACCTC
15 151 GCTCAGACCG GAACGCAGCC AAAGGGCCCC GGGCCGGCTC AGGCCATAC
20 201 GTACTACAGC GAGTGCGACG AATTTCGATT TATGCCCG CGTTCGCTGG
25 251 ACGAGGACGC CCCCGCGGAG CAGCGCACCG GGGTCCACGA CGGCCGCCTC
30 301 CGGCGCGCCC CTAAGGTGTA CTGCGGGGGG GACGAGCGCG ACGTCCTCCG
35 351 CGTGGGCCCG GAGGGCTTCT GGCCCGTCG CTTGCGCCTG TGGGGGGTG
40 401 CGGACCATGC CCCCGAGGGG TTCGACCCCA CCGTCACCGT CTTCCACGTG
45 451 TACCGACATCC TGGAGCACGT GGAACACCGG TACAGCATGC GCGCCGCCA
50 501 GCTCCACGAG CGATTTATGG ACGCCATCAC GCCCGCCGGG ACCGTATCA
55 551 CGCTTCTGGG TCTGACCCCC GAAGGCCATC GCGTCGCCGT TCACGTCTAC
60 601 GGCACGCGGC AGTACTTTA CATGAACAAG GCGGAGGTGG ATCGGCACCT
65 651 GCAGTGCCGT GCCCCGGCG ATCTCTGCGA GCGCCTGGCG GCGGCCCTGC
70 701 GCGAGTCGCC GGGGGCGTCG TTCCGCGGA TCTCCGCGGA CCACTTCGAG
75 751 GCGGAGGTGG TGGAGCGCGC CGACGTGTAC TATTACGAAA CGCGCCCGAC
80 801 CCTGTACTAC CGCGTCTTCG TGCGAAGCGG GCGCGCGCTG GCCTACCTGT
85 851 GCGACAACCTT TTGCCCCCGCG ATCAGGAAGT ACGAGGGGGG CGTCGACGCC
90 901 ACCACCCGGT TTATCCTGGA CAACCCGGGG TTTGTCACCT TCGGCTGGTA
95 951 CCGCCTCAAG CCCGGCCCGCG GGAACCGGCC GGCCCAACCG CGCCCCCCCAGA
100 1001 CGGCGTTCGG AACCTCGAGC GACGTCGAGT TTAACTGCAC GGCGGACAAC
105 1051 CTGGCCGTG AGGGGCCAT GTGTGACCTG CCGGCCTACA AGCTCATGTG
110 1101 CTTCGATATC GAATGCAAGG CCGGGGGGGG GGACGAGCTG GCCTTCCGG
115 1151 TCGCGGAACG CCCGGAAGAC CTCGTCATCC AGATCTCCTG TCTGCTCTAC
120 1201 GACCTGTCCA CCACCGCCCT CGAGCACATC CTCCTGTTT CGCTCGGATC
125 1251 CTGCGACCTC CCCGAGTCCC ACCTCAGCGA TCTCGCTCC AGGGGCCTGC
130 1301 CGGCCCCCGT CGTCCTGGAG TTTGACAGCG AATTCCGAGAT GCTGCTGGCC
135 1351 TTCATGACCT TCGTCAAGCA GTACGGCCCC GAGTTCGTGA CCGGGTACAA
140 1401 CATCATCAAC TTGACTGGC CTTCGTCCT GACCAAGCTG ACGGAGATCT

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1451 ACAAGGTCCC GCTCGACGGG TACGGGCGCA TGAACGGCCG GGGTGTGTC
1501 CGCGTGTGGG ACATCGCCA GAGCCACTT CAGAAGCGCA GCAAGATCAA
5 1551 GGTGAACGGG ATGGTGAACA TCGACATGTA CGGCATCATC ACCGACAAGG
1601 TCAAACCTCTC CAGCTACAAG CTGAACGCCG TCGCCGAGGC CGTCTTGAAG
1651 GACAAGAAGA AGGATCTGAG CTACCGCGAC ATCCCCGCCT ACTACGCCTC
10 1701 CGGGCCCGCG CAGCGCGGG TGATCGCGA GTATTGTGTG CAGGACTCGC
1751 TGCTGGTCGG GCAGCTGTT C TTCAAGTTTC TGCCGCACCT GGAGCTTCC
15 1801 GCCGTCGCGC GCCTGGCGGG CATCAACATC ACCCGCACCA TCTACGACGG
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20 1951 GCGCCCAAGC GCCCCGGCGT GCCTCGGGGG GAAGGGGAGC GGCGGGGGGA
2001 CGGGAACGGG GACGAGGATA AGGACGACGA CGAGGACGGG GACGAGGACG
25 2051 GGGACGAGCG CGAGGAGGTC GCGCGCGAGA CCGGGGGCCG GCACGTTGGG
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2151 CGTGGTGGTG TTTGACTTTG CCAGCCTGTA CCCCAGCATC ATCCAGGCC
30 2201 ACAACCTGTG CTTCAGTACG CTCTCCCTGC GGCCCAGGGC CGTCGCGCAC
2251 CTGGAGGCCG ACCGGGACTA CCTGGAGATC GAGGTGGGGG GCCGACGGCT
35 2301 GTTCTTCGTG AAGGCCACG TACCGAGAG CCTGCTGAGC ATCCTGCTGC
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40 2401 CCCCCCGAGG AGGCCGTCT CCTCGACAAG CAACAGGCCG CCATCAAGGT
2451 GGTGTGCAAC TCGGTGTACG GGTTCACCGG GGCGCAGCAC GGTCTTCTGC
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50 2701 GGCTCACGG CCGCGGGCCT GGTGGCCATG GGCGACAAGA TGGCGAGCCA
2751 CATCTCGCGC GCGCTGTTCC TCCCCCGAT CAAGCTCGAG TCGAAGAAAAA
55 2801 CGTTCACCAA GCTGCTGCTC ATCGCCAAGA AAAAGTACAT CGCGTCATC
2851 TGCGGGGGCA AGATGCTCAT CAAGGGCGTG GATCTGGTGC GCAAAACAA
2901 CTGCGCGTTT ATCAACCGCA CCTCCAGGGC CCTGGTCGAC CTGCTGTTT
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2951 ACGACGATAAC CGTATCCGGA GCGGCCGCCG CGTTAGCCGA GCGCCCCGCA
3001 GAGGAGTGGC TGGCGCGACC CCTGCCGAG GGACTGCAGG CGTTCGGGC
5 3051 CGTCCTCGTA GACGCCATC GGCGCATCAC CGACCCGGAG AGGGACATCC
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3151 AACAAAGCGCC TGGCCCACCT GACGGTGTAT TACAAGCTCA TGGCCCGCCG
10 3201 CGCGCAGGTC CCGTCCATCA AGGACCGGAT CCCGTACGTG ATCGTGGCCC
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15 3301 CTAGACGCCG CCGCCCCAGG GGACGAGCCC GCCCCCCCAG CGGCCCTGCC
3351 CTCCCCGGCC AAGGCCCCC GGGAGACGCC GTCGCATGCC GACCCCCGG
3401 GAGGCGCGTC CAAGCCCCGC AAGCTGCTGG TGTCCGAGCT GGCGGAGGAT
20 3451 CCCGGGTACG CCATCGCCCCG GGGCGTTCCG CTCAACACGG ACTATTACTT
3501 CTCGCACCTG CTGGGGCGG CCTGCGTGAC GTTCAAGGCC CTGTTGGAA
25 3551 ATAACGCCAA GATCACCGAG AGTCTGTTAA AGAGGTTTAT TCCCGAGACG
3601 TGGCACCCCC CGGACGACGT GGCGCGCGG CTCAGGGCCG CGGGGTTCCG
3651 GCCGGCGGGG GCCGGCGCTA CGGCGGAGGA AACTCGTCGA ATGTTGCATA
30 3701 GAGCCTTGA TACTCTAGCA TGA

SEQ.ID.NO. 4 Amino acid sequence of DNA polymerase for HSV2-186-M1

5 1 MFCAAGGPAS PGGKSAARAA SGFFAPHNPR GATQTAPPC RRQNFYNPHL
 51 AQTGTQPKAP GPAQRHTYYS ECDEFRFIA P RSLDEDAPAE QRTGVHDGRL
 10 101 RRAPKVYCGG DERDVLRVGP EGFWPRLRL WGGADHAPEG FDPTVTVFHV
 15 151 YDILEHVEHA YSMRAAQLHE RFMDAITPAG TVITLLGLTP EGHRVAVHVY
 20 201 GTRQYFYMNK AEVDRHLQCR APRDLCERLA AALRESPGAS FRGISADHFE
 25 251 AEVVERADVY YYETRPTLYY RVFVRSGRAL AYLCDNFCPA IRKYEGGVDA
 30 301 TTRFILDNP G FVTFGWYRLK PGRGNAPAQP RPPTAFTGSS DVEFNCTADN
 35 351 LAVEGAMCDL PAYKLMCFDI ECKAGGEDEL AFPVAERPED LVIQISCLLY
 40 401 DLSTTALEHI LLFSLGSCDL PESHLSDLAS RGLPAPVVLE FDSEFEMILLA
 45 451 FMTFVKQYGP EFVTGYNIIN FDWPFLTKL TEIYKVPLDG YGRMNNGRVF
 50 501 RVWDIGQSHF QKRSKIKVNG MVNIDMYGII TDKVKLSSYK LNAVAEAVLK
 55 551 DKKKDL SYRD IPAYYAS GPA QRGVIGEYCV QDSLLVGQLF FKFLPHLELS
 60 601 AVARLAGINI TRTTYDGQQI RVFTCLLRLA GQKGFLPDT QGRFRGLDKE
 65 651 APKRP AVPRG EGERPGDGNG DEDKDDDEDG DEDGDERE EV ARETGGRHVG
 70 701 YQGARVLDPT SGFHVDPVVV FDFASLYPSI I QAHNLCFST LSLRPEAVAH
 75 751 LEADR DYLEI EVGGRRLLFFV KAHVRESLLS ILLRDWLAMR KQIRSRI PQS
 80 801 PPEEA VLLDK QQAAIKVV CN SVYGFTGAQH GLLPCLHVAA TVTTIGREML
 85 851 LATRAYVHAR WAEFDQLLAD FPEAAGMRAP GPYSM RIIY G DTDSIFVLCR
 90 901 GLTAAGLVAM GDKMASHISR ALFLPPIKLE CEKTFTKLLL IAKKKYIGVI
 95 951 CGGKMLIKGV DLVRKNNCAF INRTSRALVD LLFYDDTVSG AAAALAERPA
 100 1001 EEWLARPLPE GLQAFGAVLV DAHRRITDPE RDIQDFVLTA ELSRHPRAYT
 105 1051 NKRLAHLTVY YKLMARRAQV PSIKDRIPYV IVAQTREVEE TVARLAALRE
 110 1101 LDAAAPGDEP APPAALPSA KRPRETPSHA DPPGGASKPR KLLVSELAED
 115 1151 PGYAIARGVP LNTDYYFSHL LGAACVTFKA LFGNNAKITE SLLKRFIPET
 120 1201 WHPPDDVAAR LRAAGFGPAG AGATAEETRR MLHRAFDL A *

SEQ.ID.NO. 5 DNA sequence of DNA polymerase gene for HSV1-KOS-M1

1 ATGTTTCCG GTGGCGCGG CCCGCTGTCC CCCGGAGGAA AGTCGGCGGC
5 51 CAGGGCGCG TCCGGTTTT TTGCGCCCGC CGGCCCTCGC GGAGCCGGCC
10 101 GGGGACCCCC GCCTTGTGG AGGCAAAACT TTTACAACCC CTACCTCGCC
15 151 CCAGTCGGGA CGCAACAGAA CCCGACCGGG CCAACCCAGC GCCATACGTA
20 201 CTATAGCGAA TGCGATGAAT TTGCGATTAT CGCCCCGCGG GTGCTGGACG
25 251 AGGATGCCCG CCCGGAGAAG CGCGCCGGGG TGACAGACGG TCACCTCAAG
30 301 CGCGCCCCCA AGGTGTACTG CGGGGGGGAC GAGCGCGACG TCCTCCGCGT
35 351 CGGGTCGGGC GGCTTCTGGC CGCGCGCTC GCGCCTGTGG GGCGGCGTGG
40 401 ACCACGCCCG GGCGGGGTTTC AACCCCACCG TCACCGTCTT TCACGTGTAC
45 451 GACATCCTGG AGAACGTGGA GCACGCGTAC GGCATGCGCG CGGCCCGAGT
50 501 CCACGCGCGG TTTATGGACG CCATCACACC GACGGGGACC GTCATCACGC
55 551 TCCTGGGCCT GACTCCGGAA GGCCACCGGG TGCCCGTTCA CGTITACGGC
60 601 ACGCGGCAGT ACTTTACAT GAACAAGGAG GAGGTTGACA GGCACCTACA
65 651 ATGCCCGGCC CCACGAGATC TCTGCGAGCG CATGGCCGG GCCCTGCGCG
70 701 AGTCCCCGGG CGCGTCGTTC CGCGGCATCT CCGCGGACCA CTTCGAGGCG
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80 801 GTTTTACCGC GTCTACGTCC GAAGCGGGCG CGTGCTGTGCG TACCTGTGCG
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135 1351 ATGACCCCTTG TGAAACAGTA CGGCCCCGAG TTGCGACCG GGTACAACAT
140 1401 CATCAACTTC GACTGGCCCT TCTTGCTGGC CAAGTTGACG GACATTTACA

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5 1551 GAACGGCATG GTAACATCG ACATGTACGG GATCATAACC GACAAGATCA
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20 1951 CCCAAGCGTC CGGCCGCAGC CCGGGAGGAC GAGGAGCCGC CAGAGGAGGA
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25 2051 AGGGCGCGCG GGAGACCGCC GGCGGCCACG TGGGTACCA GGGGGCCAGG
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30 2201 GCACGCTCTC CCTGAGGGCC GACGCAGTGG CGCACCTGGA GGCGGGCAAG
2251 GACTACCTGG AGATCGAGGT GGGGGGGCGA CGGCTGTTCT TCGTCAAGGC
35 2301 TCACGTGCGA GAGAGCCTCC TCAGCATCCT CCTGCGGGAC TGGCTCGCCA
2351 TCGGAAAGCA GATCCGCTCG CGGATTCCCC AGAGCAGCCC CGAGGAGGCC
40 2401 GTGCTCCTGG ACAAGCAGCA GGCGGCCATC AAGGTCGTGT GTAACTCGGT
2451 GTACGGGTTACCGGAGCGC ACCACGGACT CCTGCCGTGC CTGCACGTTG
2501 CCGCGACGGT GACGACCATC GGCGCGAGA TGCTGCTCGC GACCCGCGAG
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2651 ACGGGGACAC GGACTCCATA TTTGTGCTGT GCCGCGGCCT CACGGCCGCC
50 2701 GGGCTGACGG CCATGGCGA CAAGATGGCG AGCCACATCT CGCGCGCGCT
2751 GTTCTGCCCG CCCATCAAAC TCGAGTGCAGA AAAGACGTTACCAAGCTGC
55 2801 TGCTGATCGC CAAGAAAAAG TACATCGCG TCATCTACGG GGGTAAGATG
2851 CTCATCAAGG GCGTGGATCT GGTGCGAAA AACAACTGCG CGTTTATCAA
2901 CCGCACCTCC AGGGCCCTGG TCGACCTGCT GTTTACGAC GATACCGTAT
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2951 CCGGAGCGGC CGCCGCGTTA GCCGAGCGCC CCGCAGAGGA GTGGCTGGCG
3001 CGACCCCTGC CCGAGGGACT GCAGGCCTTC GGGGCCGTCC TCGTAGACGC
5 3051 CCATCGCGC ATCACCGACC CGGAGAGGGGA CATCCAGGAC TTTGTCTCA
3101 CCGCCGAACG GAGCAGACAC CCGCGCGCGT ACACCAACAA GCGCCTGGCC
3151 CACCTGACGG TGTATTACAA GCTCATGGCC CGCCGCGCGC AGGTCCCGTC
10 3201 CATCAAGGAC CGGATCCCGT ACGTGATCGT GGCCCAGACC CGCGAGGTAG
3251 AGGAGACGGT CGCGCGGCTG GCCGCCCTCC GCGAGCTAGA CGCCGCCGCC
15 3301 CCAGGGGACG AGCCCGCCCC CCCCCGCGGCC CTGCCCTCCC CGGCCAAGCG
3351 CCCCCGGGAG ACGCCGTCGC ATGCCGACCC CCCGGGAGGC GCGTCCAAGC
3401 CCCGCAAGCT GCTGGTGTCC GAGCTGGCCG AGGATCCGC ATACGCCATT
20 3451 GCCCACGGCG TCGCCCTGAA CACGGACTAT TACTTCTCCC ACCTGTTGGG
3501 GGCGGCGTGC GTGACATTCA AGGCCCTGTT TGGGAATAAC GCCAAGATCA
25 3551 CCGAGAGTCT GTTAAAAAGG TTTATTCCCG AAGTGTGGCA CCCCCCGGAC
3601 GACGTGGCCG CGCGGCTCCG GGCCGCAGGG TTCGGGGCGG TGGGTGCCGG
3651 CGCTACGGCG GAGGAAACTC GTCGAATGTT GCATAGAGCC TTTGATACTC
30 3701 TAGCATGA

SEQ.ID.NO. 6 Amino acid sequence of DNA polymerase for HSV1-KOS-M1

1 MFSGGGGPLS PGGKSAARAA SGFFAPAGPR GAGRGPPLC RQNFYNPYLA
 5 51 PVGTQQKPTG PTQRHTYYSE CDEFRFIAPR VLDEDAPPEK RAGVHDGHLK
 10 101 RAPKVYCGGD ERDVLRVGSG GFWPRRSRLW GGVDHAPAGF NPTVTVFHVY
 15 151 DILENVEHAY GMRAAQFHAR FMDAITPTGT VITLLGLTPE GHRVAHVYVG
 20 201 TRQYFYMNKE EVDRHLQCRA PRDLCEMAA ALRESPGASF RGISADHFEA
 25 251 EVVERTDVYY YETRPALFYR VYVRSGRVLS YLCDNFCPAI KKYEYGGVDA
 30 301 TRFILDNPGF VTFGWYRLKP GRNNNTLAQPR APMAFGTSSD VEFNCTADNL
 35 351 AIEGGMSDLP AYKLMCFDIE CKAGGEDELA FPVAGHPEDL VIQISCLLYD
 40 401 LSTTALEHVL LFSLGSCDLP ESHLNELAAR GLPTPVVLEF DSEFEMLLAF
 45 451 MTLVKQYGPE FVTGYNINF DWPFLLAKLT DIYKVPLDGY GRMNNGRVFR
 50 501 VWDIGQSHFQ KRSKIKVNGM VNIDMYGIIT DKIKLSSYKL NAVAЕAVLKD
 55 551 KKKDLSYRDI PAYYAAGPAQ RGVIGEYCIQ DSLLVGQLFF KFLPHLELSA
 60 601 VARLAGINIT RTIYDGQQIR VFTCLLRLAD QKGFILPDTQ GRFRGAGGEA
 65 651 PKRPAAAARED EERPEEEGED EDEREEGGGE REPEGARETA GRHVGYQGAR
 70 701 VLDPTSGFHV NPVVVFDFAS LYPSTIQAHN LCFSTLSLRA DAVAHLLEAGK
 75 751 DYLEIEVGGR RLFFVKAHVR ESLLSILLRD WLAMRKQIRS RIPQSSPEEA
 80 801 VLLDKQQAAI KVVCNSVYGF TGAQHGLPC LHVAATVTTI GREMLLATRE
 85 851 YVHARWAAFE QLLADFPEAA DMRAPGPYSM RTIYGDTDSI FVLCRGLTAA
 90 901 GLTAMGDKMA SHISRALFLP PIKLECEKTF TKLLIAKKK YIGVIYGGKM
 95 951 LIKGVDLVRK NNCAFINRTS RALVDLLFYD DTVSGAAAAL AERPAEEWLA
 100 1001 RPLPEGLQAF GAVLVDAHRR ITDPERDIQD FVLTAELSRH PRAYTNKRLA
 105 1051 HLTVYYKLMA RRAQVPSIKD RIPYVIVAQT REVEETVARL AALRELDAAA
 110 1101 PGDEPAPPAA LPSPAKRPRE TPSHADPPGG ASKPRKLLVS ELAEDPAYAI
 115 1151 AHGVALNTDY YFSHILLGAAC VTFKALFGNN AKITESLLKR FIPFVWHPPD
 120 1201 DVAARLRAAG FGAVGAGATA EETRRMLHRA FDTLA*

SEQ.ID.NO. 7 DNA sequence of HSV polymerase gene for HSV1-F-M1

5	1	ATGTTTCCG GTGGCGCGG CCCGCTGTCC CCCGGAGGAA AGTCGGCGC
	51	CAGGGCGCG TCCGGTTTT TTGCGCCCGC CGGCCCTCGC GGAGCCGGCC
	101	GGGGACCCCC GCCTGCTTG AGGCAAAACT TTTACAACCC CTACCTCGCC
10	151	CCAGTCGGGA CGCAACAGAA GCCGACCGGG CCAACCCAGC GCCATACGTA
	201	CTATAGCGAA TGCGATGAAT TTGCGATTCA CGCCCGCGG GTGCTGGACG
15	251	AGGATGCCCG CCCGGAGAAG CGCGCCGGG TGCACGACGG TCACCTCAAG
	301	CGCGCCCCCA AGGTGTACTG CGGGGGGGAC GAGCGCGACG TCCTCCGCGT
	351	CGGGTCGGGC GGCTCTGGC CGCGCGCTC GGCCTGTGG GGCGCGTGG
20	401	ACCACGCCCGG GGCGGGGTTTC AACCCCACCG TCACCGTCTT TCACGTGTAC
	451	GACATCCTGG AGAACGTGGA GCACGCGTAC GGCAATGCGCG CGGCCCCAGTT
25	501	CCACGCGCGG TTTATGGACG CCATCACACC GACGGGGACC GTCATCACGC
	551	TCCTGGGCCT GACTCCGGAA GGCCACCGGG TGGCCGTTCA CGTTTACGGC
	601	ACGCGGCAGT ACTTTTACAT GAACAAGGAG GAGGTCGACA GGCACCTACA
30	651	ATGCCCGGCC CCACGAGATC TCTGCGAGCG CATGGCCGCG GCCCTGCGCG
	701	AGTCCCCGGG CGCGTCGTTTC CGCGGCATTT CGCGGGACCA CTTCGAGGCG
35	751	GAGGTGGTGG AGCGCACCGA CGTGTACTAC TACGAGACGC GCCCCGCTCT
	801	GTTTTACCGC GTCTACGTCC GAAGCGGGCG CGTGCTGTGCG TACCTGTGCG
	851	ACAACCTCTG CCCGGCCATC AAGAAGTACG AGGGTGGGGT CGACGCCACC
40	901	ACCCGGTTCA TCCTGGACAA CCCCCGGGTTTC GTCACCTTCG GCTGGTACCG
	951	TCTCAAACCG GGCGGAAACA ACACGCTAGC CCAGCCCGCGG GCCCCGATGG
45	1001	CCTTCGGGAC ATCCAGCGAC GTCGAGTTTA ACTGTACGGC GGACAACCTG
	1051	GCCATCGAGG GGGGCATGAG CGACCTACCG GCATACAAGC TCATGTGCTT
	1101	CGATATCGAA TGCAAGGCGG GGGGGGAGGA CGAGCTGGCC TTTCCGGTGG
50	1151	CCGGGCACCC GGAGGACCTG GTCATCCAGA TATCCTGTCT GCTCTACGAC
	1201	CTGTCCACCA CCGCCCTGGA GCACGTCCCTC CTGTTTCGCG TCGGTTCCCTG
55	1251	CGACCTCCCC GAATCCCACC TGAACGAGCT GGCGGCCAGG GGCCTGCCA
	1301	CGCCCGTGGT TCTGGAATTC GACAGCGAAT TCGAGATGCT GTTGGCCTTC
	1351	ATGACCCCTTG TGAAACAGTA CGGCCCCGAG TTCGTGACCG GGTACAACAT
60	1401	CATCAACTTC GACTGGCCCT TCTTGCTGGC CAAGCTGACG GACATTTACA
	1451	AGGTCCCCCT GGACGGGTAC GGCGCATGA ACGGCCGGGG CGTGTTCGCG
65	1501	GTGTGGGACA TAGGCCAGAG CCACCTCCAG AAGCGCAGCA AGATAAAGGT
	1551	GAACGGCATG GTGAACATCG ACATGTACGG GATTATAACC GACAAGATCA

	1601	AGCTCTCGAG CTACAAGCTC AACGCCGTGG CCGAAGCCGT CCTGAAGGAC
5	1651	AAGAAGAAGG ACCTGAGCTA TCGCGACATC CCCGCCTACT ACGCCGCCGG
	1701	GCCCCGCGAA CGCGGGGTGA TCGGCGAGTA CTGCATACAG GATTCCCTGC
	1751	TGGTGGGCCA GCTGTTTTT AAGTTTTGC CCCATCTGGA GCTCTCGGCC
10	1801	GTCGGCCGCT TGGCGGGTAT TAACATCACC CGCACCATCT ACGACGGCCA
	1851	GCAGATCCGC GTCTTACGT GCCTGCTGCG CCTGGCCGAC CAGAAGGGCT
15	1901	TTATTCTGCC GGACACCCAG GGGCGATTAA GGGCGGGCGG GGGGGAGGCG
	1951	CCCAAGCGTC CGGCCGCAGC CCGGGAGGAC GAGGAGCGC CAGAGGAGGA
	2001	GGGGGAGGAC GAGGACGAAC GCGAGGAGGG CGGGGGCGAG CGGGAGCCGG
20	2051	AGGGCGCGCG GGAGACCGCC GGCCGGCACG TGGGGTACCA GGGGGCCAGG
	2101	GTCCTTGACC CCACTTCCGG GTTTCATGTG AACCCCGTGG TGGTGTTCGA
25	2151	CTTTGCCAGC CTGTACCCCCA GCATCATCCA GGCCCACAAAC CTGTGCTTCA
	2201	GCACGCTCTC CCTGAGGGCC GACGCAGTGG CGCACCTGGA GGCGGGCAAG
	2251	GAATACCTGG AGATCGAGGT GGGGGGGCGA CGGCTGTTCT TCGTCAAGGC
30	2301	TCACGTGCGA GAGAGCCTCC TCAGCATCCT CCTGCAGGAC TGGCTCGCCA
	2351	TGCGAAAGCA GATCCGCTCG CGGATTCCCC AGAGCAGCCC CGAGGAGGCC
35	2401	GTGCTCCTGG ACAAGCAGCA GGCCGCCATC AAGGTCGTGT GTAACTCGGT
	2451	TTACGGGTTAC CGGGGAGCGC AGCACGGACT CCTGCCGTGC CTGCACGTTG
	2501	CCGCGACGGT GACGACCATC GGCGCGAGA TGCTGCTCGC GACCCGCGAG
40	2551	TACGTCCACG CGCGCTGGGC GGCCCTCGAA CAGCTCCTGG CCGATTCCCC
	2601	GGAGGCGGCC GACATGCGCG CCCCCGGGCC CTATTCCATG CGCATCATCT
45	2651	ACGGGGACAC GGACTCCATC TTTGTGCTGT GCCGCAGGCCT CACGGCCGCC
	2701	GGGCTGACGG CGTGCGCGA CAAGATGGCG AGCCACATCT CGCGCGCGCT
	2751	GTTTCTGTCC CCCATCAAAC TCGAGTGCAGA AAAGACGTTC ACCAAGCTGC
50	2801	TGCTGATCGC CAAGAAAAAG TACATCGCG TCATCTACGG GGGTAAGATG
	2851	CTCATCAAGG GCGTGGATCT GGTGCGCAA AACAACTGCG CGTTTATCAA
55	2901	CCGCACCTCC AGGGCCCTGG TCGACCTGCT GTTTTACGAC GATAACGTAT
	2951	CCGGAGCGGC CGCCCGCGTTA GCCGAGCGCC CGCAGAGGA GTGGCTGGCG
	3001	CGACCCCTGC CGAGGGACT GCAGGCGTTC GGGGCCGTCC TCGTAGACGC
60	3051	CCATCGCGC ATCACCGACC CGGAGAGGGA CATCCAGGAC TTTGTCCCTCA
	3101	CCGCCGAACG GAGCAGACAC CGCGCGCGT ACACCAACAA GCGCCTGGCC
65	3151	CACCTGACGG TGTATTACAA GCTCATGCC CGCCCGCGC AGGTCCCCTC
	3201	CATCAAGGAC CGGATCCCGT ACGTGATCGT GGCCCAGACC CGCGAGGTAG

3251 AGGAGACGGT CGCGCGGCTG GCGGCCCTCC GCGAGCTCGA CGCCGCCGCC
3301 CCAGGGGACG AGCCCAGCCC CCCCAGGGCC CTGCCCTCCC CGGCCAAGCG
5 3351 CCCCCGGGAG ACGCCGTTGC ATGCCGACCC CCCGGGAGGC GCGTCCAAGC
3401 CCCGCAAGCT GCTGGTGTCC GAGCTGGCCG AGGATCCCAG ATACGCCATT
10 3451 GCCCACGGCG TCGCCCTGAA CACGGACTAT TACTTCTCCC ACCTGTTGGG
3501 GGCAGGGTGC GTGACATTCA AGGCCCTGTT TGGGAATAAC GCCAAGATCA
3551 CCGAGAGTCT GTTAAAAAGG TTTATTCCCG AAGTGTGGCA CCCCCCGGAC
15 3601 GACGTGGCCG CGCGGCTCCG GGCGCAGGG TTCGGGGCGG TGGGTGCCGG
3651 CGCTACGGCG GAGGAAACTC GTCGAATGTT GCATAGAGCC TTTGATACTC
3701 TAGCATGA

SEQ.ID.NO. 8 Amino acid sequence of DNA polymerase for HSV1-F-M1

1 MFSGGGGPLS PGGKSAARAA SGFFAPAGPR GAGRGPPLC RQNFYNPYLA
 5 51 PVTQQKPTG PTQRHTYYSE CDEFRFIAPR VLDEDAPPEK RAGVHDGHLK
 10 101 RAPKVYCGGD ERDVLRVGSG GFWPRRSRLW GGVDHAPAGF NPTVTVFHVV
 15 151 DILENVEHAY GMRAAQFHAR FMDAITPTGT VITLLGLTPE GHRVAVHVY
 20 201 TRQYFYMNKE EVDRHLQCRA PRDLCEMAA ALRESPGASF RGISADHFEA
 25 251 EVVERTDVYY YETRPALFYR VYVRSGRVLS YLCDNFCPAI KKYEGGVDAT
 30 301 TRFILDNPFG VTFGWYRLKP GRNNTLAQPR APMAFGTSSD VEFNCTADNL
 35 351 AIEGGMSDLP AYKLMCFDIE CKAGGEDELA FPVAGHPEDL VIQISCLLYD
 40 401 LSTTALEHVL LFSLGSCDLP ESHLNELAAR GLPTPVVLEF DSEFEMLLAF
 45 451 MTLVKQYGP E FVTGYNINF DWPFLAKLT DIYKVPLDGY GRMNGRGVFR
 50 501 VWDIGQSHFQ KRSKIKVNGM VNIDMYGIT DKIKLSSYKL NAVAЕAVLKD
 55 551 KKKDLSYRDI PAYYAAGPAQ RGIVIGEYCIQ DSLLVGQLFF KFLPHLELSA
 60 601 VARLAGINIT RTTYDGQQIR VFTCLLRLAD QKGFIPLDTQ GRFRGGGEA
 65 651 PKRPAAARED EERPEEEGED EDEREEGGGE REPEGARETA GRHVGYQGAR
 70 701 VLDPTSGFHV NPVVVFDFAS LYSIIQAHN LCFSTLSLRA DAVAHLEAGK
 75 751 DYLEIEVGGR RLFFVKAHVR ESSLSSILLRD WLAMRKQIRS RIPQSSPEEA
 80 801 VLLDKQQAAI KVVCNSVYGF TGAQHGLLPC LHVAATVTTI GREMLLATRE
 85 851 YVHARWAAFE QLLADFPEAA DMRAPGPYSM RIIYGDTDSI FVLCRGLTAA
 90 901 GLTAVGDKMA SHISRALFLS PIKLECEKTF TKLLLIAKKK YIGVIYGGKM
 95 951 LIKGVDLVRK NNCAFINRTS RALV DLLFYD DTVSGAAAAL AERPAEEWLA
 100 1001 RPLPEGLQAF GAVLVDAHRR ITDPERDIQD FVLTAELSRH PRAYTNKRLA
 105 1051 HLTVYYKLMA RRAQVPSIKD RIPYVIVAQT REVEETVARL AALRELDAAA
 110 1101 PGDEPAPPAA LPSPAKRPRE TPLHADPPGG ASKPRKLLVS ELAEDPAYAI
 115 1151 AHGVALNTDY YFSHLLGAAC VTFKALFGNN AKITESLLKR FIPEVWHPPD
 120 1201 DVAARLRAAG FGAVGAGATA EETRRMLHRA FDTLA*

SEQ.ID.NO. 9 DNA sequence of HSV polymerase gene for HSV1-DJL-M1

1 ATGTTTCCG GTGGCGCGG CCCGCTGTCC CCCGGAGGAA AGTCGGCGC
 5 51 CAGGGCGCG TCCGGTTTT TTGCGCCCGC CGGCCCTCGC GGAGCCGGCC
 10 101 GGGGACCCCC GCCTTGTGG AGGCAAAACT TTTACAACCC CTACCTCGCC
 15 151 CCAGTCGGGA CGCAACAGAA GCCGACCGGG CCAACCCAGC GCCATACGTA
 20 201 CTATAGCGAA TGCGATGAAT TTGATTATCGAT CGCCCCGGG GTGCTGGACG
 25 251 AGGATGCCCG CCCGGAGAAG CGCGCCGGG TGACGACGG TCACCTCAAG
 30 301 CGCGCCCCCA AGGTGTACTG CGGGGGGAC GAGCGCGACG TCCTCCGCGT
 35 351 CGGGTCGGGC GGCTTCTGGC CGCGCGCTC GCGCTGTGG GGCGCGTGG
 40 401 ACCACGCCCG GGCGGGGTTCAACCCACCG TCACCGTCTT TCACGTGTAT
 45 451 GACATCCTGG AGAACGTGGA GCACCGTAC GGCAATGCGCG CGGCCAGTT
 50 501 CCACGCGCGG TTATGGACG CCATCACACC GACGGGGACC GTCATCACCG
 55 551 TCCTGGGCCT GACTCCGAA GGCCACCGGG TGGCCGTTCA CGTTTACGGC
 60 601 ACGCGGCAGT ACTTTACAT GAACAAGGAG GAGGTTGACA GGACACCTACA
 65 651 ATGCCGCGCC CCACGAGATC TCTGCGAGCG CATGGCCGCG GCCCTGCGCG
 70 701 AGTCCCCGGG CGCGTCGTTCCCGGCATCT CCGCGGACCA CTTCGAGGCG
 75 751 GAGGTGGTGG AGCGCACCGA CGTGTACTAC TACGAGACGC GCCCGCTCT
 80 801 GTTTTACCGC GTCTACGTCC GAAGCGGGCG CGTGTGTCG TACCTGTGCG
 85 851 ACAACTTCTG CCCGGCCATC AAGAAAGTACG AGGGTGGGGT CGACGCCACC
 90 901 ACCCGGTCA TCCTGGACAA CCCGGGGTTCA GTCACCTTCG GCTGGTACCG
 95 951 TCTCAAACCG GGCGGAACA ACACGCTAGC CCAGCCGCGG GCCCGATGG
 100 1001 CCTTCGGGAC ATCCAGCGAT GTCGAGTTA ACTGTACGGC GGACAACCTG
 105 1051 GCCATCGAGG GGGGCATGAG CGACCTACCG GCATACAAGC TCATGTGCTT
 110 1101 CGATATCGAA TGCAAGGCAGG GGGGGGAGGA CGAGCTGGCC TTTCCGGTGG
 115 1151 CCGGGCACCC GGAGGACCTG GTCATCCAGA TATCCTGTCT GCTCTACGAC
 120 1201 CTGTCCACCA CCGCCCTGGA GCACGTCTC CTGTTTCGC TCGGTTCTG
 125 1251 CGACCTCCCC GAATCCCACC TGAACGAGCT GGCGGCCAGG GGCGCTGCCA
 130 1301 CGCCCGTGGT TCTGGAATTGACAGCGAAT TCGAGATGCT GTTGGCCCTC
 135 1351 ATGACCCCTTG TGAAACAGTA CGGCCCCGAG TTCTGACCG GGTACAACAT
 140 1401 AATCAACTTC GACTGGCCCT TCTTGCTGGC CAAGCTGACG GACATTAC

1451 AGGTCCCCCT GGACGGGTAC GGCGCATGA ACGGCCGGGG CGTGTTCGC
1501 GTGTGGGACA TAGGCCAGAG CCACTTCAG AAGCGCAGCA AGATAAAGGT
5 1551 GAACGGCATG GTAACATCG ACATGTACGG GATTATAACC GACAAGATCA
1601 AGCTCTCGAG CTACAAGCTC AACGCCGTGG CCGAAGCCGT CCTGAAGGAC
10 1651 AAGAAGAAGG ACCTGAGCTA TCGCGACATC CCCACCTACT ACGCCGCCGG
1701 GCCCGCGCAA CGCGGGGTGA TCGCGAGTA CTGCATACAG GATTCCCTGC
1751 TGGTGGGCCA GCTGTTTTT AAGTTTTGC CCCATCTGGA GCTCTCGGCC
15 1801 GTCGCGCGCT TGGCGGGTAT TAACATCACC CGCACCATCT ACGACGGCCA
1851 GCAGATCCGC GTCTTACGT GCCTGCTGCG CCTGGCCGAC CAGAAGGGCT
20 1901 TTATTCTGCC GGACACCCAG GGGCGATTIA GGGGCGCCGG GGGGGAGGCG
1951 CCCAAGCGTC CGGCCGCAGC CCGGGAGGAC GAGGAGCGGC CAGAGGAGGA
2001 GGGGGAGGAC GAGAACGAAC GCGAGGAGGG CGGGGGCGAG CGGGAGCCGG
25 2051 AGGGCGCGCG GGAGACCGCC GGCGGCACG TGGGGTACCA GGGGGCCAGG
2101 GTCCTTGACC CCACTTCCGG GTTTCACGTG AACCCCGTGG TGGTGTTCGA
30 2151 CTTTGCCAGC CTGTACCCCCA GCATCATCCA GGCCCACAAC CTGTGCTTCA
2201 GCACGCTCTC CCTGAGGGCC GACGCAGTGG CGCACCTGGA GGCGGGCAAG
2251 GACTACCTGG AGATCGAGGT GGGGGGGCGA CGGCTTCT TCGTCAAGGC
35 2301 TCACGTGCGA GAGAGCCTCC TCAGCATCCT CCTGCGGGAC TGGCTCGCCA
2351 TCGGAAAGCA GATCCGCTCG CGGATTCCCC AGAGCAGCCC CGAGGAGGCC
40 2401 GTGCTCCTGG ACAAGCAGCA GGCGCCATC AAGGTCGTGT GTAACCTCGGT
2451 TTACGGGTTACCGGGAGCGC AGCACGGACT CCTGCCGTGC CTGCACGTTG
2501 CCGCGACGGT GACGACCATC GGCGCGAGA TGCTGCTCGC GACCCGCGAG
45 2551 TACGTCCACG CGCGCTGGC GGCCTTCGAA CAGCTCTGG CCGATTCCCC
2601 GGAGGCGGCC GACATGCGCG CCCCCGGGCC CTATTCCATG CGCATCATCT
50 2651 ACGGGGACAC GGACTCCATA TTTGTGCTGT GCCGCGGCCT CACGGCCGCC
2701 GGGCTGACGG CCGTGGCGA CAAGATGGCG AGCCACATCT CGCGCGCGCT
2751 GTTTCTGCC CCCATCAAAC TCGAGTGCAG AAAGACGTTACCAAGCTGC
55 2801 TGCTGATCGC CAAGAAAAAG TACATCGGCG TCATCTACGG GGGTAAGATG
2851 CTCATCAAGG GCGTGGATCT GGTGCGAAA AACAACTGCG CGTTTATCAA
60 2901 CCGCACCTCC AGGGCCCTGG TCGACCTGCT GTTTACGAC GATACCGTAT

2951 CCGGAGCGGC CGCCGCGTTA GCCGAGCGCC CCGCAGAGGA GTGGCTGGCG
5 3001 CGACCCCTGC CCGAGGGACT GCAGGCCTTC GGGGCCGTCC TCGTAGACGC
3051 CCATCGGCAC ATCACCGACC CGGAGAGGGA CATCCAGGAC TTTGTTCTCA
3101 CCGCCGAACG GAGCAGACAC CCGCGCGCGT ACACCAACAA GCGCCTGGCC
10 3151 CACCTGACGG TGTATTACAA GCTCATGGCC CGCCGCGCGC AGGTCCCGTC
3201 CATCAAGGAC CGGATCCCGT ACGTGATCGT GGCCCAGACC CGCGAGGTAG
3251 AGGAGACGGT CGCGCGGCTG GCCGCCCTCC GCGAGCTAGA CGCCGCCGCC
15 3301 CCAGGGGACG AGCCCGCCCC CCCCAGGGCC CTGCCCTCCC CGGCCAAGCG
3351 CCCCCGGGAG ACGCCGTCGC CTGCCGACCC CCCGGGAGGC GCGTCCAAGC
20 3401 CCCGCAAGCT GCTGGTGTCC GAGCTGGCCG AGGATCCCGC ATACGCCATT
3451 GCCCACGGCG TCGCCCTGAA CACGGACTAT TACTTCTCCC ACCTGTTGGG
3501 GCGGGCGTGC GTGACATTCA AGGCCCTGTT TGGGAATAAC GCCAAGATCA
25 3551 CCGAGAGTCT GTTAAAAAGG TTTATTCCCG AAGTGTGGCA CCCCCCGGAC
3601 GACGTGGCCG CGCGGCTCCG GACCGCAGGG TTCGGGGCGG TGGGTGCCGG
30 3651 CGCTACGGCG GAGGAAACTC GTCGAATGTT GCATAGAGCC TTTGATACTC
3701 TAGCATGA

SEQ.ID.NO. 10 Amino acid sequence of DNA polymerase for HSV1-DJL-M1

1 MFSGGGGPLS PGGKSAARAA SGFFAPAGPR GAGRGPPL RQNFYNPYLA
 5 51 PVGTQQKPTG PTQRHTYYSE CDEFRFIAPR VLDEDAPPEK RAGVHDGHLK
 101 RAPKVYCGGD ERDVLRVGSG GFWPRRSRLW GGVDHAPAGF NPTVTVFHVY
 151 DILENVEHAY GMRAAQFHAR FMDAITPTGT VITLLGLTPE GHRVAVHVY
 10 201 TRQYFYMNKE EVDRHLQCRA PRDLCERMAA ALRESPGASF RGISADHFEA
 251 EVVERTDVYY YETRPALFYR VYVRSGRVLS YLCDNFCPAI KKYEggVDA
 15 301 TRFILDNPGF VTFGWYRLKP GRNNNTLAQPR APMAFGTSSD VEFNCTADNL
 351 AIEGGMSDLP AYKLMCFDIE CKAGGEDELA FPVAGHPEDL VIQISCLLYD
 401 LSTTALEHVL LFSLGSCDLP ESHLNELAAR GLPTPVVLEF DSEFEMLLAF
 20 451 MTLVKQYGP EFTGYNIINF DWPFLLAKLT DIYKVPLDGY GRMNGRGVFR
 501 VWDIGQSHFQ KRSKIKVNGM VNIDMYGIIT DKIKLSSYKL NAVAЕAVLKD
 25 551 KKKDLSYRDI PTYYAAGPAQ RGVIGEYCIQ DSLLVGQLFF KFLPHLELSA
 601 VARLAGINIT RTIYDGQQIR VFTCLLRLAD QKGFLPDTQ GRFRGAGGEA
 651 PKRPAAAARED EERPEEEGED ENEREEGGGE REPEGARETA GRHVGYQGAR
 30 701 VLDPTSGFHV NPVVVFDFAS LYPSIIQAHN LCFSTLSLRA DAVAHLEAGK
 751 DYLEIEVGGR RLFFVKAHVR ESLLSILLRD WLAMRKQIRS RIPQSSPEEA
 35 801 VLLDKQQAAI KVVCNSVYGF TGAQHGLLPC LHVAATVTTI GREMILLATRE
 851 YVHARWAAFE QLLADFPEAA DMRAPGPYSM RIYGDTSI FVLCRGLTAA
 901 GLTAVGDKMA SHISRALFLP PIKLECEKTF TKLLLIAKKK YIGVITYGGKM
 40 951 LIKGVDLVRK NNCAFINRTS RALVDLLFYD DTVSGAAAAL AERPAEEWLA
 1001 RPLPEGLQAF GAVLVDAHRR ITDPERDIQD FVLTAELSRH PRAYTNKRLA
 45 1051 HLTVYYKLMA RRAQVPSIKD RJPYVIVAQT REVEETVARL AALRELDAAA
 1101 PGDEPAPPAA LPSPAKRPRE TPSPADPPGG ASKPRKLLVS ELAEDPAYAI
 1151 AHGVALNTDY YFSHLLGAAC VTFKALFGNN AKITESLLKR FIPEVWHPPD
 50 1201 DVAARLRTAG FGAVGAGATA EETRRMLHRA FDTLA*

SEQ.ID.NO. 11 DNA sequence of DNA polymerase gene for HMCV-AD169-M1

1 ATGTTTTCA ACCCGTATCT GAGCGGCGGC GTGACCGGCG GTGCGGTCGC
5 51 GGGTGGCCGG CGTCAGCGTT CGCAGCCGG CTCCGCGCAG GGCTCGGGCA
10 101 AGCGGCCGCC ACAGAAACAG TTTTGAGA TCGTGCGCG AGGTGTATG
15 151 TTGACGGTC AGACGGGTT GATCAAGCAT AAGACGGGAC GGCTGCCTCT
20 201 CATGTTCTAT CGAGAGATTA AACATTTGTT GAGTCATGAC ATGGTTGGC
25 251 CGTGTCCCTTG GCGCGAGACC CTGGTGGTC GCGTGGTGGG ACCTATTGCT
30 301 TTTCACACCT ACGATCAGAC GGACGCCGTG CTCTTCTTCG ACTCGCCGA
35 351 AAACGTGTCG CCGCGCTATC GTCAGCATCT GGTGCCTTCG GGGAACGTGT
40 401 TGCCTTCTT CGGGGCCACA GAACACGGCT ACAGTATCTG CGTCAACGTT
45 451 TTCCGGCAGC GCAGCTACTT TTACTGTGAG TACAGCGACA CCGATAGGCT
50 501 GCGTGAGGTC ATTGCCAGCG TGGCGAACT AGTGCCGAA CCGCGGACGC
55 551 CATA CGCCGT GTCTGTCACG CCGGCCACCA AGACCTCCAT CTATGGGTAC
60 601 GGGACGCGAC CCGTGCCCGA TTTGCAGTGT GTGTCTATCA GCAACTGGAC
65 651 CATGCCAGA AAAATCGCG AGTATCTGCT GGAGCAGGGT TTTCCCGTGT
70 701 ACGAGGTCCG TGTGGATCCG CTGACCGTGT TGGTCATCGA TCGGCGGATC
75 751 ACCACGTTCG GCTGGTGCTC CGTGAATCGT TACGACTGGC GGCAGCAGGG
80 801 TCGCGCGTCG ACTTGTGATA TCGAGGTAGA CTGCGATGTC TCTGACCTGG
85 851 TGGCTGTGCC CGACGACAGC TCGTGGCCGC GCTATCGATG CCTGTCCCTC
90 901 GATATCGAGT GCATGAGCGG CGAGGGTGGT TTTCCCTGCG CCGAGAACGTC
95 951 CGATGACATT GTCATTCAAGA TCTCGTGCCT GTGCTACGAG ACGGGGGGAA
100 1001 ACACCGCCGT GGATCAGGGG ATCCCAAACG GGAACGATGG TCGGGGCTGC
105 1051 ACTTCGGAGG GTGTGATCTT TGGGCACTCG GGTCTTCATC TCTTACGAT
110 1101 CGGCACCTGC GGGCAGGTGG GCCCAGACGT GGACGTCTAC GAGTTCCCTT
115 1151 CCGAATACGA GCTGCTGCTG GGCTTTATGC TTTTCTTCA ACGGTACGCG
120 1201 CCGGCCTTIG TGACCGGTTA CAACATCAAC TCTTTGACT TGAAGTACAT
125 1251 CCTCACGCGT CTCGAGTACC TGTATAAGGT GGACTCGCAG CGCTCTGCA
130 1301 AGTTGCCTAC GGCGCAGGGC GGCGTTCT TTTTACACAG CCCCAGCGTG
135 1351 GGTTTAAGC GGCAAGTACGC CGCCGTTTT CCCTCGGCTT CTCACAACAA
140 1401 TCCGGCCAGC ACGGCCGCCA CCAAGGTGTA TATTGCGGGT TCGGTGGTTA

1451 TCGACATGTA CCCTGTATGC ATGGCCAAGA CTAACTCGCC CAACTATAAG
1501 CTCAACACTA TGGCCGAGCT TTACCTGCGG CAACGCAAGG ATGACCTGTC
5 1551 TTACAAGGAC ATCCCGCGTT GTTTCGTGGC TAATGCCGAG GGCCGCGCCC
1601 AGGTAGGCCG TTACTGTCTG CAGGACGCCG TATTGGTGCG CGATCTGTC
10 1651 AACACCATTA ATTTCACTA CGAGGCCGGG GCCATCGCGC GGCTGGCTAA
1701 AATTCCGTTG CGGCGTGTCA TCTTGACGG ACAGCAGATC CGTATCTACA
1751 CCTCGCTGCT GGACGAGTGC GCCTGCCGCG ATTTTATCCT GCCCAACCAC
15 1801 TACAGCAAAG GTACGACGGT GCCCGAAACG AATAGCGTTG CTGTGTCACC
1851 TAACGCTGCT ATCATCTCTA CCGCCGCTGT GCCCGGCGAC GCGGGTTCTG
20 1901 TGGCGGCTAT GTTCAGATG TCGCCGCCCT TGCAATCTGC GCCGTCCAGT
1951 CAGGACGGCG TTTCACCCGG CTCCGGCAGT AACAGTAGTA GCAGCGTCGG
2001 CGTTTCAGC GTCGGCTCCG GCAGTAGTGG CGGCCTCGGC GTTTCCAACG
25 2051 ACAATCACGG CGCCGGCGGT ACTGCGGCGG TTTCGTACCA GGGCGCCACG
2101 GTGTTTGAGC CCGAGGTGGG TTACTACAAC GACCCGTGG CCGTGTTCGA
30 2151 CTTTGCCAGC CTCTACCCCTT CCATCATCAT GGCCCACAAC CTCTGCTACT
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2251 TACAGCGTCA CGCTAGAGAA CGGCGTGACC CACCGCTTG TGCCTGCTTC
35 2301 GGTGCGCGTC TCGGTGCTCT CGGAAC TGCTCAAGTGG GTTTCGCAGC
2351 GGCCTGCCGT GCGGAATGC ATGCGCGAGT GTCAAGACCC TGTGCGCCGT
40 2401 ATGCTGCTCG ACAAGGAACA GATGGCGCTC AAAGTAACGT GCAACGCTTT
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3601 CTGTCGCCCG TCTTTCCCGG CGGCGAAACC GCGCGCAAAGG ACAAGTTTT
30 3651 GCACATGGTG CTGCCGCCGGC GCTTGCACCTT GGAGCCGGCT TTTCTGCCGT
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SEQ. ID. NO. 12 Amino acid sequence of DNA polymerase for HCMV-AD169-M1

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 10 151 FGQRQSYFYCE YSDTDRLREV IASVGEVPE PRTPYAVSVT PATKTSIYGY
 201 GTRPVPDLCV VSISNWTMAR KIGEYLLEQG FPVYEVVDP LTRLVIDRRI
 251 TTFGWCSVNR YDWRQQGRAS TCDIEVDCDV SDLVAVPDDS SWPRYRCLSF
 15 301 DIECMSSGEGG FPCAEKSDDI VIQISCVCYE TGGNTAVDQG IPNGNDGRGC
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 20 401 PAFVTGYNIN SFDLKYILTR LEYLYKVDSQ RFCKLPTAQQ GRFFLHSPAV
 451 GFKRQYAAAF PSASHNNPAS TAATKVYIAG SVVIDMYPVC MAKTNSPNYK
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 50 1151 GEPAKKRARK PPSAVCNYEV AEDPSYVREH GPPIHADKYF EQVLKAVTNV
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Figure 6

SEQ.ID.NO.13 Amino acid sequence of DNA polymerase for HCMV-AD169

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 25 251 TTFGWCSVNR YDWRQQGRAS TCDIEVDCDV SDLVAVPDDS SWPRYRCLSF
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SEQUENCE LISTING

<110> Homa, Fred
Wathen, Michael
Hopkins, Todd
Thomsen, Darrell

<120> A Method for Treating Herpes Virus

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tga						3723	

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 <212> PRT
 <213> herpes simplex

<400> 4

Met Phe Cys Ala Ala Gly Gly Pro Ala Ser Pro Gly Gly Lys Ser Ala
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Thr Gln Thr Ala Pro Pro Cys Arg Arg Gln Asn Phe Tyr Asn Pro
 35 40 45

His Leu Ala Gln Thr Gly Thr Gln Pro Lys Ala Pro Gly Pro Ala Gln
 50 55 60

Arg His Thr Tyr Tyr Ser Glu Cys Asp Glu Phe Arg Phe Ile Ala Pro
 65 70 75 80

Arg Ser Leu Asp Glu Asp Ala Pro Ala Glu Gln Arg Thr Gly Val His
 85 90 95

Asp Gly Arg Leu Arg Arg Ala Pro Lys Val Tyr Cys Gly Gly Asp Glu
 100 105 110

Arg Asp Val Leu Arg Val Gly Pro Glu Gly Phe Trp Pro Arg Arg Leu
 115 120 125

Arg Leu Trp Gly Gly Ala Asp His Ala Pro Glu Gly Phe Asp Pro Thr
 130 135 140

Val Thr Val Phe His Val Tyr Asp Ile Leu Glu His Val Glu His Ala

145	150	155	160
Tyr Ser Met Arg Ala Ala Gln Leu His Glu Arg Phe Met Asp Ala Ile			
165	170	175	
Thr Pro Ala Gly Thr Val Ile Thr Leu Leu Gly Leu Thr Pro Glu Gly			
180	185	190	
His Arg Val Ala Val His Val Tyr Gly Thr Arg Gln Tyr Phe Tyr Met			
195	200	205	
Asn Lys Ala Glu Val Asp Arg His Leu Gln Cys Arg Ala Pro Arg Asp			
210	215	220	
Leu Cys Glu Arg Leu Ala Ala Leu Arg Glu Ser Pro Gly Ala Ser			
225	230	235	240
Phe Arg Gly Ile Ser Ala Asp His Phe Glu Ala Glu Val Val Glu Arg			
245	250	255	
Ala Asp Val Tyr Tyr Glu Thr Arg Pro Thr Leu Tyr Tyr Arg Val			
260	265	270	
Phe Val Arg Ser Gly Arg Ala Leu Ala Tyr Leu Cys Asp Asn Phe Cys			
275	280	285	
Pro Ala Ile Arg Lys Tyr Glu Gly Gly Val Asp Ala Thr Thr Arg Phe			
290	295	300	
Ile Leu Asp Asn Pro Gly Phe Val Thr Phe Gly Trp Tyr Arg Leu Lys			
305	310	315	320
Pro Gly Arg Gly Asn Ala Pro Ala Gln Pro Arg Pro Pro Thr Ala Phe			
325	330	335	
Gly Thr Ser Ser Asp Val Glu Phe Asn Cys Thr Ala Asp Asn Leu Ala			
340	345	350	
Val Glu Gly Ala Met Cys Asp Leu Pro Ala Tyr Lys Leu Met Cys Phe			
355	360	365	
Asp Ile Glu Cys Lys Ala Gly Gly Glu Asp Glu Leu Ala Phe Pro Val			
370	375	380	
Ala Glu Arg Pro Glu Asp Leu Val Ile Gln Ile Ser Cys Leu Leu Tyr			
385	390	395	400
Asp Leu Ser Thr Thr Ala Leu Glu His Ile Leu Leu Phe Ser Leu Gly			
405	410	415	
Ser Cys Asp Leu Pro Glu Ser His Leu Ser Asp Leu Ala Ser Arg Gly			
420	425	430	
Leu Pro Ala Pro Val Val Leu Glu Phe Asp Ser Glu Phe Glu Met Leu			
435	440	445	
Leu Ala Phe Met Thr Phe Val Lys Gln Tyr Gly Pro Glu Phe Val Thr			
450	455	460	
Gly Tyr Asn Ile Ile Asn Phe Asp Trp Pro Phe Val Leu Thr Lys Leu			
465	470	475	480

Thr Glu Ile Tyr Lys Val Pro Leu Asp Gly Tyr Gly Arg Met Asn Gly
 485 490 495
 Arg Gly Val Phe Arg Val Trp Asp Ile Gly Gln Ser His Phe Gln Lys
 500 505 510
 Arg Ser Lys Ile Lys Val Asn Gly Met Val Asn Ile Asp Met Tyr Gly
 515 520 525
 Ile Ile Thr Asp Lys Val Lys Leu Ser Ser Tyr Lys Leu Asn Ala Val
 530 535 540
 Ala Glu Ala Val Leu Lys Asp Lys Lys Asp Leu Ser Tyr Arg Asp
 545 550 555 560
 Ile Pro Ala Tyr Tyr Ala Ser Gly Pro Ala Gln Arg Gly Val Ile Gly
 565 570 575
 Glu Tyr Cys Val Gln Asp Ser Leu Leu Val Gly Gln Leu Phe Phe Lys
 580 585 590
 Phe Leu Pro His Leu Glu Leu Ser Ala Val Ala Arg Leu Ala Gly Ile
 595 600 605
 Asn Ile Thr Arg Thr Ile Tyr Asp Gly Gln Gln Ile Arg Val Phe Thr
 610 615 620
 Cys Leu Leu Arg Leu Ala Gly Gln Lys Gly Phe Ile Leu Pro Asp Thr
 625 630 635 640
 Gln Gly Arg Phe Arg Gly Leu Asp Lys Glu Ala Pro Lys Arg Pro Ala
 645 650 655
 Val Pro Arg Gly Glu Gly Glu Arg Pro Gly Asp Gly Asn Gly Asp Glu
 660 665 670
 Asp Lys Asp Asp Asp Glu Asp Gly Asp Glu Asp Gly Asp Glu Arg Glu
 675 680 685
 Glu Val Ala Arg Glu Thr Gly Gly Arg His Val Gly Tyr Gln Gly Ala
 690 695 700
 Arg Val Leu Asp Pro Thr Ser Gly Phe His Val Asp Pro Val Val Val
 705 710 715 720
 Phe Asp Phe Ala Ser Leu Tyr Pro Ser Ile Ile Gln Ala His Asn Leu
 725 730 735
 Cys Phe Ser Thr Leu Ser Leu Arg Pro Glu Ala Val Ala His Leu Glu
 740 745 750
 Ala Asp Arg Asp Tyr Leu Glu Ile Glu Val Gly Gly Arg Arg Leu Phe
 755 760 765
 Phe Val Lys Ala His Val Arg Glu Ser Leu Leu Ser Ile Leu Leu Arg
 770 775 780
 Asp Trp Leu Ala Met Arg Lys Gln Ile Arg Ser Arg Ile Pro Gln Ser
 785 790 795 800
 Pro Pro Glu Glu Ala Val Leu Leu Asp Lys Gln Gln Ala Ala Ile Lys
 805 810 815

Val Val Cys Asn Ser Val Tyr Gly Phe Thr Gly Ala Gln His Gly Leu
 820 825 830
 Leu Pro Cys Leu His Val Ala Ala Thr Val Thr Thr Ile Gly Arg Glu
 835 840 845
 Met Leu Leu Ala Thr Arg Ala Tyr Val His Ala Arg Trp Ala Glu Phe
 850 855 860
 Asp Gln Leu Leu Ala Asp Phe Pro Glu Ala Ala Gly Met Arg Ala Pro
 865 870 875 880
 Gly Pro Tyr Ser Met Arg Ile Ile Tyr Gly Asp Thr Asp Ser Ile Phe
 885 890 895
 Val Leu Cys Arg Gly Leu Thr Ala Ala Gly Leu Val Ala Met Gly Asp
 900 905 910
 Lys Met Ala Ser His Ile Ser Arg Ala Leu Phe Leu Pro Pro Ile Lys
 915 920 925
 Leu Glu Cys Glu Lys Thr Phe Thr Lys Leu Leu Leu Ile Ala Lys Lys
 930 935 940
 Lys Tyr Ile Gly Val Ile Cys Gly Gly Lys Met Leu Ile Lys Gly Val
 945 950 955 960
 Asp Leu Val Arg Lys Asn Asn Cys Ala Phe Ile Asn Arg Thr Ser Arg
 965 970 975
 Ala Leu Val Asp Leu Leu Phe Tyr Asp Asp Thr Val Ser Gly Ala Ala
 980 985 990
 Ala Ala Leu Ala Glu Arg Pro Ala Glu Glu Trp Leu Ala Arg Pro Leu
 995 1000 1005
 Pro Glu Gly Leu Gln Ala Phe Gly Ala Val Leu Val Asp Ala His
 1010 1015 1020
 Arg Arg Ile Thr Asp Pro Glu Arg Asp Ile Gln Asp Phe Val Leu
 1025 1030 1035
 Thr Ala Glu Leu Ser Arg His Pro Arg Ala Tyr Thr Asn Lys Arg
 1040 1045 1050
 Leu Ala His Leu Thr Val Tyr Tyr Lys Leu Met Ala Arg Arg Ala
 1055 1060 1065
 Gln Val Pro Ser Ile Lys Asp Arg Ile Pro Tyr Val Ile Val Ala
 1070 1075 1080
 Gln Thr Arg Glu Val Glu Glu Thr Val Ala Arg Leu Ala Ala Leu
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 Arg Glu Leu Asp Ala Ala Pro Gly Asp Glu Pro Ala Pro Pro
 1100 1105 1110
 Ala Ala Leu Pro Ser Pro Ala Lys Arg Pro Arg Glu Thr Pro Ser
 1115 1120 1125
 His Ala Asp Pro Pro Gly Gly Ala Ser Lys Pro Arg Lys Leu Leu

1130	1135	1140
Val Ser Glu Leu Ala Glu Asp	Pro Gly Tyr Ala Ile	Ala Arg Gly
1145	1150	1155
Val Pro Leu Asn Thr Asp Tyr	Tyr Phe Ser His Leu	Leu Gly Ala
1160	1165	1170
Ala Cys Val Thr Phe Lys Ala	Leu Phe Gly Asn Asn	Ala Lys Ile
1175	1180	1185
Thr Glu Ser Leu Leu Lys Arg	Phe Ile Pro Glu Thr	Trp His Pro
1190	1195	1200
Pro Asp Asp Val Ala Ala Arg	Leu Arg Ala Ala Gly	Phe Gly Pro
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Arg Ala Phe Asp Thr Leu Ala		
1235	1240	
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 <212> PRT
 <213> herpes simplex

<400> 6

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Gly Arg Gly Pro Pro Pro Cys Leu Arg Gln Asn Phe Tyr Asn Pro Tyr
 35 40 45

Leu Ala Pro Val Gly Thr Gln Gln Lys Pro Thr Gly Pro Thr Gln Arg
 50 55 60

His Thr Tyr Tyr Ser Glu Cys Asp Glu Phe Arg Phe Ile Ala Pro Arg
 65 70 75 80

Val Leu Asp Glu Asp Ala Pro Pro Glu Lys Arg Ala Gly Val His Asp
 85 90 95

Gly His Leu Lys Arg Ala Pro Lys Val Tyr Cys Gly Gly Asp Glu Arg
 100 105 110

Asp Val Leu Arg Val Gly Ser Gly Gly Phe Trp Pro Arg Arg Ser Arg
 115 120 125

Leu Trp Gly Gly Val Asp His Ala Pro Ala Gly Phe Asn Pro Thr Val

130	135	140
Thr Val Phe His Val Tyr Asp Ile Leu Glu Asn Val Glu His Ala Tyr		
145	150	155
Gly Met Arg Ala Ala Gln Phe His Ala Arg Phe Met Asp Ala Ile Thr		
165	170	175
Pro Thr Gly Thr Val Ile Thr Leu Leu Gly Leu Thr Pro Glu Gly His		
180	185	190
Arg Val Ala Val His Val Tyr Gly Thr Arg Gln Tyr Phe Tyr Met Asn		
195	200	205
Lys Glu Glu Val Asp Arg His Leu Gln Cys Arg Ala Pro Arg Asp Leu		
210	215	220
Cys Glu Arg Met Ala Ala Leu Arg Glu Ser Pro Gly Ala Ser Phe		
225	230	235
Arg Gly Ile Ser Ala Asp His Phe Glu Ala Glu Val Val Glu Arg Thr		
245	250	255
Asp Val Tyr Tyr Tyr Glu Thr Arg Pro Ala Leu Phe Tyr Arg Val Tyr		
260	265	270
Val Arg Ser Gly Arg Val Leu Ser Tyr Leu Cys Asp Asn Phe Cys Pro		
275	280	285
Ala Ile Lys Lys Tyr Glu Gly Gly Val Asp Ala Thr Thr Arg Phe Ile		
290	295	300
Leu Asp Asn Pro Gly Phe Val Thr Phe Gly Trp Tyr Arg Leu Lys Pro		
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Gly Arg Asn Asn Thr Leu Ala Gln Pro Arg Ala Pro Met Ala Phe Gly		
325	330	335
Thr Ser Ser Asp Val Glu Phe Asn Cys Thr Ala Asp Asn Leu Ala Ile		
340	345	350
Glu Gly Gly Met Ser Asp Leu Pro Ala Tyr Lys Leu Met Cys Phe Asp		
355	360	365
Ile Glu Cys Lys Ala Gly Glu Asp Glu Leu Ala Phe Pro Val Ala		
370	375	380
Gly His Pro Glu Asp Leu Val Ile Gln Ile Ser Cys Leu Leu Tyr Asp		
385	390	395
Leu Ser Thr Thr Ala Leu Glu His Val Leu Leu Phe Ser Leu Gly Ser		
405	410	415
Cys Asp Leu Pro Glu Ser His Leu Asn Glu Leu Ala Ala Arg Gly Leu		
420	425	430
Pro Thr Pro Val Val Leu Glu Phe Asp Ser Glu Phe Glu Met Leu Leu		
435	440	445
Ala Phe Met Thr Leu Val Lys Gln Tyr Gly Pro Glu Phe Val Thr Gly		
450	455	460

Tyr Asn Ile Ile Asn Phe Asp Trp Pro Phe Leu Leu Ala Lys Leu Thr
 465 470 475 480
 Asp Ile Tyr Lys Val Pro Leu Asp Gly Tyr Gly Arg Met Asn Gly Arg
 485 490 495
 Gly Val Phe Arg Val Trp Asp Ile Gly Gln Ser His Phe Gln Lys Arg
 500 505 510
 Ser Lys Ile Lys Val Asn Gly Met Val Asn Ile Asp Met Tyr Gly Ile
 515 520 525
 Ile Thr Asp Lys Ile Lys Leu Ser Ser Tyr Lys Leu Asn Ala Val Ala
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 Glu Ala Val Leu Lys Asp Lys Lys Lys Asp Leu Ser Tyr Arg Asp Ile
 545 550 555 560
 Pro Ala Tyr Tyr Ala Ala Gly Pro Ala Gln Arg Gly Val Ile Gly Glu
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 Tyr Cys Ile Gln Asp Ser Leu Leu Val Gly Gln Leu Phe Phe Lys Phe
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 Leu Pro His Leu Glu Leu Ser Ala Val Ala Arg Leu Ala Gly Ile Asn
 595 600 605
 Ile Thr Arg Thr Ile Tyr Asp Gly Gln Gln Ile Arg Val Phe Thr Cys
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 Leu Leu Arg Leu Ala Asp Gln Lys Gly Phe Ile Leu Pro Asp Thr Gln
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 Thr Ala Gly Arg His Val Gly Tyr Gln Gly Ala Arg Val Leu Asp Pro
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 Thr Ser Gly Phe His Val Asn Pro Val Val Val Phe Asp Phe Ala Ser
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 Leu Tyr Pro Ser Ile Ile Gln Ala His Asn Leu Cys Phe Ser Thr Leu
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 Ser Leu Arg Ala Asp Ala Val Ala His Leu Glu Ala Gly Lys Asp Tyr
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 Leu Glu Ile Glu Val Gly Gly Arg Arg Leu Phe Phe Val Lys Ala His
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 Val Arg Glu Ser Leu Leu Ser Ile Leu Leu Arg Asp Trp Leu Ala Met
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 Arg Lys Gln Ile Arg Ser Arg Ile Pro Gln Ser Ser Pro Glu Glu Ala
 785 790 795 800

Val Leu Leu Asp Lys Gln Gln Ala Ala Ile Lys Val Val Cys Asn Ser
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 Val Tyr Gly Phe Thr Gly Ala Gln His Gly Leu Leu Pro Cys Leu His
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 Val Ala Ala Thr Val Thr Ile Gly Arg Glu Met Leu Leu Ala Thr
 835 840 845
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Leu Ala Pro Val Gly Thr Gln Gln Lys Pro Thr Gly Pro Thr Gln Arg
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His Thr Tyr Tyr Ser Glu Cys Asp Glu Phe Arg Phe Ile Ala Pro Arg
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Val Leu Asp Glu Asp Ala Pro Pro Glu Lys Arg Ala Gly Val His Asp
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Gly His Leu Lys Arg Ala Pro Lys Val Tyr Cys Gly Gly Asp Glu Arg
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Asp Val Leu Arg Val Gly Ser Gly Gly Phe Trp Pro Arg Arg Ser Arg

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Gly Met Arg Ala Ala Gln Phe His Ala Arg Phe Met Asp Ala Ile Thr		
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Pro Thr Gly Thr Val Ile Thr Leu Leu Gly Leu Thr Pro Glu Gly His		
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Arg Val Ala Val His Val Tyr Gly Thr Arg Gln Tyr Phe Tyr Met Asn		
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Lys Glu Glu Val Asp Arg His Leu Gln Cys Arg Ala Pro Arg Asp Leu		
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Cys Glu Arg Met Ala Ala Leu Arg Glu Ser Pro Gly Ala Ser Phe		
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Arg Gly Ile Ser Ala Asp His Phe Glu Ala Glu Val Val Glu Arg Thr		
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Asp Val Tyr Tyr Tyr Glu Thr Arg Pro Ala Leu Phe Tyr Arg Val Tyr		
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Val Arg Ser Gly Arg Val Leu Ser Tyr Leu Cys Asp Asn Phe Cys Pro		
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Ala Ile Lys Lys Tyr Glu Gly Gly Val Asp Ala Thr Thr Arg Phe Ile		
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Leu Asp Asn Pro Gly Phe Val Thr Phe Gly Trp Tyr Arg Leu Lys Pro		
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Thr Ser Ser Asp Val Glu Phe Asn Cys Thr Ala Asp Asn Leu Ala Ile		
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Glu Gly Gly Met Ser Asp Leu Pro Ala Tyr Lys Leu Met Cys Phe Asp		
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Ile Glu Cys Lys Ala Gly Gly Glu Asp Glu Leu Ala Phe Pro Val Ala		
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Leu Ser Thr Thr Ala Leu Glu His Val Leu Leu Phe Ser Leu Gly Ser		
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Cys Asp Leu Pro Glu Ser His Leu Asn Glu Leu Ala Ala Arg Gly Leu		
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Pro Thr Pro Val Val Leu Glu Phe Asp Ser Glu Phe Glu Met Leu Leu		
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Ala Phe Met Thr Leu Val Lys Gln Tyr Gly Pro Glu Phe Val Thr Gly
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 35 40 45

Leu Ala Pro Val Gly Thr Gln Gln Lys Pro Thr Gly Pro Thr Gln Arg
 50 55 60

His Thr Tyr Tyr Ser Glu Cys Asp Glu Phe Arg Phe Ile Ala Pro Arg
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Val Leu Asp Glu Asp Ala Pro Pro Glu Lys Arg Ala Gly Val His Asp
 85 90 95

Gly His Leu Lys Arg Ala Pro Lys Val Tyr Cys Gly Gly Asp Glu Arg

100	105	110
Asp Val Leu Arg Val Gly Ser Gly Gly Phe Trp Pro Arg Arg Ser Arg		
115	120	125
Leu Trp Gly Gly Val Asp His Ala Pro Ala Gly Phe Asn Pro Thr Val		
130	135	140
Thr Val Phe His Val Tyr Asp Ile Leu Glu Asn Val Glu His Ala Tyr		
145	150	155
Gly Met Arg Ala Ala Gln Phe His Ala Arg Phe Met Asp Ala Ile Thr		
165	170	175
Pro Thr Gly Thr Val Ile Thr Leu Leu Gly Leu Thr Pro Glu Gly His		
180	185	190
Arg Val Ala Val His Val Tyr Gly Thr Arg Gln Tyr Phe Tyr Met Asn		
195	200	205
Lys Glu Glu Val Asp Arg His Leu Gln Cys Arg Ala Pro Arg Asp Leu		
210	215	220
Cys Glu Arg Met Ala Ala Leu Arg Glu Ser Pro Gly Ala Ser Phe		
225	230	235
Arg Gly Ile Ser Ala Asp His Phe Glu Ala Glu Val Val Glu Arg Thr		
245	250	255
Asp Val Tyr Tyr Glu Thr Arg Pro Ala Leu Phe Tyr Arg Val Tyr		
260	265	270
Val Arg Ser Gly Arg Val Leu Ser Tyr Leu Cys Asp Asn Phe Cys Pro		
275	280	285
Ala Ile Lys Lys Tyr Glu Gly Val Asp Ala Thr Thr Arg Phe Ile		
290	295	300
Leu Asp Asn Pro Gly Phe Val Thr Phe Gly Trp Tyr Arg Leu Lys Pro		
305	310	315
Gly Arg Asn Asn Thr Leu Ala Gln Pro Arg Ala Pro Met Ala Phe Gly		
325	330	335
Thr Ser Ser Asp Val Glu Phe Asn Cys Thr Ala Asp Asn Leu Ala Ile		
340	345	350
Glu Gly Gly Met Ser Asp Leu Pro Ala Tyr Lys Leu Met Cys Phe Asp		
355	360	365
Ile Glu Cys Lys Ala Gly Gly Glu Asp Glu Leu Ala Phe Pro Val Ala		
370	375	380
Gly His Pro Glu Asp Leu Val Ile Gln Ile Ser Cys Leu Leu Tyr Asp		
385	390	395
Leu Ser Thr Thr Ala Leu Glu His Val Leu Leu Phe Ser Leu Gly Ser		
405	410	415
Cys Asp Leu Pro Glu Ser His Leu Asn Glu Leu Ala Ala Arg Gly Leu		
420	425	430

Pro Thr Pro Val Val Leu Glu Phe Asp Ser Glu Phe Glu Met Leu Leu
 435 440 445
 Ala Phe Met Thr Leu Val Lys Gln Tyr Gly Pro Glu Phe Val Thr Gly
 450 455 460
 Tyr Asn Ile Ile Asn Phe Asp Trp Pro Phe Leu Leu Ala Lys Leu Thr
 465 470 475 480
 Asp Ile Tyr Lys Val Pro Leu Asp Gly Tyr Gly Arg Met Asn Gly Arg
 485 490 495
 Gly Val Phe Arg Val Trp Asp Ile Gly Gln Ser His Phe Gln Lys Arg
 500 505 510
 Ser Lys Ile Lys Val Asn Gly Met Val Asn Ile Asp Met Tyr Gly Ile
 515 520 525
 Ile Thr Asp Lys Ile Lys Leu Ser Ser Tyr Lys Leu Asn Ala Val Ala
 530 535 540
 Glu Ala Val Leu Lys Asp Lys Lys Asp Leu Ser Tyr Arg Asp Ile
 545 550 555 560
 Pro Thr Tyr Tyr Ala Ala Gly Pro Ala Gln Arg Gly Val Ile Gly Glu
 565 570 575
 Tyr Cys Ile Gln Asp Ser Leu Leu Val Gly Gln Leu Phe Phe Lys Phe
 580 585 590
 Leu Pro His Leu Glu Leu Ser Ala Val Ala Arg Leu Ala Gly Ile Asn
 595 600 605
 Ile Thr Arg Thr Ile Tyr Asp Gly Gln Gln Ile Arg Val Phe Thr Cys
 610 615 620
 Leu Leu Arg Leu Ala Asp Gln Lys Gly Phe Ile Leu Pro Asp Thr Gln
 625 630 635 640
 Gly Arg Phe Arg Gly Ala Gly Glu Ala Pro Lys Arg Pro Ala Ala
 645 650 655
 Ala Arg Glu Asp Glu Glu Arg Pro Glu Glu Gly Glu Asp Glu Asn
 660 665 670
 Glu Arg Glu Glu Gly Gly Glu Arg Glu Pro Glu Gly Ala Arg Glu
 675 680 685
 Thr Ala Gly Arg His Val Gly Tyr Gln Gly Ala Arg Val Leu Asp Pro
 690 695 700
 Thr Ser Gly Phe His Val Asn Pro Val Val Val Phe Asp Phe Ala Ser
 705 710 715 720
 Leu Tyr Pro Ser Ile Ile Gln Ala His Asn Leu Cys Phe Ser Thr Leu
 725 730 735
 Ser Leu Arg Ala Asp Ala Val Ala His Leu Glu Ala Gly Lys Asp Tyr
 740 745 750
 Leu Glu Ile Glu Val Gly Gly Arg Arg Leu Phe Phe Val Lys Ala His
 755 760 765

Val Arg Glu Ser Leu Leu Ser Ile Leu Leu Arg Asp Trp Leu Ala Met
 770 775 780
 Arg Lys Gln Ile Arg Ser Arg Ile Pro Gln Ser Ser Pro Glu Glu Ala
 785 790 795 800
 Val Leu Leu Asp Lys Gln Gln Ala Ala Ile Lys Val Val Cys Asn Ser
 805 810 815
 Val Tyr Gly Phe Thr Gly Ala Gln His Gly Leu Leu Pro Cys Leu His
 820 825 830
 Val Ala Ala Thr Val Thr Thr Ile Gly Arg Glu Met Leu Leu Ala Thr
 835 840 845
 Arg Glu Tyr Val His Ala Arg Trp Ala Ala Phe Glu Gln Leu Leu Ala
 850 855 860
 Asp Phe Pro Glu Ala Ala Asp Met Arg Ala Pro Gly Pro Tyr Ser Met
 865 870 875 880
 Arg Ile Ile Tyr Gly Asp Thr Asp Ser Ile Phe Val Leu Cys Arg Gly
 885 890 895
 Leu Thr Ala Ala Gly Leu Thr Ala Val Gly Asp Lys Met Ala Ser His
 900 905 910
 Ile Ser Arg Ala Leu Phe Leu Pro Pro Ile Lys Leu Glu Cys Glu Lys
 915 920 925
 Thr Phe Thr Lys Leu Leu Leu Ile Ala Lys Lys Tyr Ile Gly Val
 930 935 940
 Ile Tyr Gly Gly Lys Met Leu Ile Lys Gly Val Asp Leu Val Arg Lys
 945 950 955 960
 Asn Asn Cys Ala Phe Ile Asn Arg Thr Ser Arg Ala Leu Val Asp Leu
 965 970 975
 Leu Phe Tyr Asp Asp Thr Val Ser Gly Ala Ala Ala Leu Ala Glu
 980 985 990
 Arg Pro Ala Glu Glu Trp Leu Ala Arg Pro Leu Pro Glu Gly Leu Gln
 995 1000 1005
 Ala Phe Gly Ala Val Leu Val Asp Ala His Arg Arg Ile Thr Asp
 1010 1015 1020
 Pro Glu Arg Asp Ile Gln Asp Phe Val Leu Thr Ala Glu Leu Ser
 1025 1030 1035
 Arg His Pro Arg Ala Tyr Thr Asn Lys Arg Leu Ala His Leu Thr
 1040 1045 1050
 Val Tyr Tyr Lys Leu Met Ala Arg Arg Ala Gln Val Pro Ser Ile
 1055 1060 1065
 Lys Asp Arg Ile Pro Tyr Val Ile Val Ala Gln Thr Arg Glu Val
 1070 1075 1080
 Glu Glu Thr Val Ala Arg Leu Ala Ala Leu Arg Glu Leu Asp Ala

1085	1090	1095
Ala Ala Pro Gly Asp Glu Pro	Ala Pro Pro Ala Ala	Leu Pro Ser
1100	1105	1110
Pro Ala Lys Arg Pro Arg Glu	Thr Pro Ser Pro Ala	Asp Pro Pro
1115	1120	1125
Gly Gly Ala Ser Lys Pro Arg	Lys Leu Leu Val Ser	Glu Leu Ala
1130	1135	1140
Glu Asp Pro Ala Tyr Ala Ile	Ala His Gly Val Ala	Leu Asn Thr
1145	1150	1155
Asp Tyr Tyr Phe Ser His Leu	Leu Gly Ala Ala Cys	Val Thr Phe
1160	1165	1170
Lys Ala Leu Phe Gly Asn Asn	Ala Lys Ile Thr Glu	Ser Leu Leu
1175	1180	1185
Lys Arg Phe Ile Pro Glu Val	Trp His Pro Pro Asp	Asp Val Ala
1190	1195	1200
Ala Arg Leu Arg Thr Ala Gly	Phe Gly Ala Val Gly	Ala Gly Ala
1205	1210	1215
Thr Ala Glu Glu Thr Arg Arg	Met Leu His Arg Ala	Phe Asp Thr
1220	1225	1230
Leu Ala		
1235		

<210> 11
 <211> 3729
 <212> DNA
 <213> herpes simplex

<400> 11		
atgtttttca acccgatatct gagcggcggt gtgaccggcg gtgcggtcgc gggtgccgg	60	
cgtcagcggtt cgcagcccggtt ctccgcgcag ggctcgggca agcggccgccc acagaaacag	120	
ttttgcaga tcgtgccgcg aggtgtcatg ttcgacggtc agacggggttt gatcaagcat	180	
aagacgggac ggctgcctct catgttctat cgagagatta aacattttttt gagtcatgac	240	
atggtttggc cgtgtccttg gcgcgagacc ctgggggttgcgtgggtttt acctattcgat	300	
tttcacacactt acgatcagac ggacgcgttgc ctcttcttgc actcgcccgaa aaacgtgtcg	360	
ccgcgtatc gtcagcatct ggtgccttcg gggAACGTGT tgctttttttt cggggccaca	420	
gaacacggctt acagttatctg cgtcaacgtt ttccggcagc gcagctactt ttactgtgag	480	
tacagcgaca ccgataggctt gcgtgagggtt attgcgcggcg tggggcaactt agtgcggcggaa	540	
ccgcggacgc catacgccgt gtctgtcactg ccggccacca agacctccat ctatgggtac	600	
gggacgcgac ccgtgccccgtt tttgcagtgtt gtgtctatca gcaactggac catggccaga	660	
aaaatcgccg agtatctgtt ggagcagggtt tttcccggtt acgagggtccg tttggatccg	720	

ctgacgcgtt	tggtcatcga	tcggcggatc	accacgttcg	gctggtgatc	cgtgaatcgt	780
tacgactggc	ggcagcaggg	tcgcgcgtcg	acttgtata	tcgaggtaga	ctgcgatgtc	840
tctgacctgg	tggctgtgcc	cgacgacagc	tcgtggccgc	gctatcgatg	cctgtccttc	900
gatatcgagt	gcatgagcgg	cgaggggtgg	tttccctgcg	ccgagaagtc	cgatgacatt	960
gtcattcaga	tctcgtgcgt	gtgctacgag	acggggggaa	acaccggcgt	ggatcagggg	1020
atcccaaacg	ggaacgatgg	tcggggctgc	acttcggagg	gtgtgatctt	tgggcactcg	1080
ggtcttcata	tctttacgat	ccgcacactgc	gggcagggtgg	gcccagacgt	ggacgtctac	1140
gagttccctt	ccgaatacga	gctgctgctg	ggctttatgc	ttttctttca	acggtacgcg	1200
ccggcctttg	tgaccgggta	caacatcaac	tctttgact	tgaagtacat	cctcagcgt	1260
ctcgagtacc	tgtataaggt	ggactcgcag	cgcttctgca	agttgcctac	ggcgcagggc	1320
ggccgtttct	ttttacacag	ccccggcgtg	ggtttaagc	ggcagtacgc	cgccgcttt	1380
ccctcggtt	ctcacaacaa	tccggccagc	acggccgcca	ccaaggtgta	tattgcgggt	1440
tcgggtggta	tcgacatgta	ccctgtatgc	atggccaaga	ctaactcgcc	caactataag	1500
ctcaacacta	tggccgagct	ttacctgcgg	caacgcaagg	atgacctgtc	ttacaaggac	1560
atcccggtt	gtttcgtggc	taatgcccag	ggccgcgccc	aggtaggccg	ttactgtctg	1620
caggacgccc	tattggtgcg	cgatctgttc	aacaccatta	attttcaacta	cgaggccggg	1680
gccatcgccg	ggctggctaa	aattccgttg	cggtgtca	tctttgacgg	acagcagatc	1740
cgtatctaca	cctcgctgct	ggacgagtgc	gcctgcccgc	attttacct	gcccaaccac	1800
tacagcaaag	gtacgacggt	gcccggaaacg	aatagcggtt	ctgtgtcacc	taacgctgct	1860
atcatctcta	ccgcccgtgt	gccccggcgc	gcgggttctg	tggcggctat	gtttcagatg	1920
tcgcccctt	tgcaatctgc	gccgtccagt	caggacggcg	tttcacccgg	ctccggcagt	1980
aacagtagta	gcagcgtcgg	cgttttcagc	gtcggctccg	gcagtagtgg	cggtgtcggc	2040
gtttccaacg	acaatcacgg	cgccggcggt	actgcggcgg	tttcgtacca	gggcgccacg	2100
gtgtttgagc	ccgaggtggg	ttactacaac	gaccccggtt	ccgtgttcga	ctttgccagc	2160
ctctaccctt	ccatcatcat	ggccccacaac	ctctgctact	ccaccctgct	ggtgccgggt	2220
ggcgagtacc	ctgtggaccc	cgccgacgta	tacagcgtca	cgctagagaa	cggtgtcacc	2280
caccgctttg	tgcgtgttcc	ggtgccgcgtc	tcgggtgtct	cggaactgct	caacaagtgg	2340
gtttcgcagc	ggcgtgccgt	gctcgaaatgc	atgcgcgagt	gtcaagaccc	tgtgcgcgt	2400
atgctgctcg	acaaggaaca	gatggcgctc	aaagtaacgt	gcaacgcttt	ctacggttt	2460
accggcgcgc	tgaacggtat	gatggcggt	ctgccccatcg	ccgcccagcat	cacgcgcac	2520
ggtcgcgaca	tgctagagcg	cacggcgcgg	ttcatcaaag	acaactttc	agagccgtgt	2580

tttttgcaca attttttaa tcaggaagac tatgtatgg gaacgcggga gggggattcg 2640
 gaggagagca gcgcgttacc ggaggggctc gaaacatcgta cagggggctc gaacgaacgg 2700
 cgggtggagg cgccgggtcat ctacgggac acggacagcg tgtttgcgtccg ctttcgtggc 2760
 ctgacgcccgc aggctctggt ggccgcgtggg cccagcctgg cgcaactacgt gacggccgt 2820
 ctttttgtgg agccccgtcaa gctggagttt gaaaaggctt tcgtctctct tatgtatgatc 2880
 tgcaagaaac gttacatcgga caaaagtggag ggccgcctcggt gtctgagcat gaagggcgt 2940
 gatctggtgc gcaagacggc ctgcgagttc gtcaagggcg tcacgcgtga cgtccctctcg 3000
 ctgctctttg aggatcgcgaa ggtctcgaa gcagccgtgc gcctgtcgccg cctctcaactc 3060
 gatgaagtca agaagtacgg cgtgccacgc ggtttctggc gatatcttacg ccgcttggtg 3120
 caggcccgcg acgatctgtta cctgcaccgt gtgcgtgtcg aggacctggc gctttcgctcg 3180
 gtgcgtctcta aggacatctc gctgtaccgt caatctaacc tgccgcacat tgccgtcatt 3240
 aagcgattgg cggcccggttc tgaggagcta ccctcggtcg gggatcgggt cttttacgtt 3300
 ctgacggcgc cccgtgtccg gacggcccg cagggttccct ccgacaacgg tgattctgtta 3360
 accgcggcgccg tggtttcccg gtcggacgcg attgatggca cggacgacga cgctgacggc 3420
 ggcggggtag aggagagcaa caggagagga ggagagccgg caaagaagag ggccgcggaaa 3480
 ccaccgtccgg ccgtgtgcaaa ctacgaggta gccgaagatc cgagctacgt ggcgcgacac 3540
 ggcgtgcccata ttacgcccga caagtacttt gagcaggatc tcaaggctgt aactaacgtg 3600
 ctgtcgccccg tctttcccg cggcgaaacc gcgcgcagg acaagttttt gcacatggtg 3660
 ctgcccggc gcttgcactt ggagccggct tttctgcccgt acagtgtcaa ggccacgaa 3720
 tgctgttga 3729

<210> 12
 <211> 1242
 <212> PRT
 <213> herpes simplex

<400> 12

Met Phe Phe Asn Pro Tyr Leu Ser Gly Gly Val Thr Gly Gly Ala Val
 1 5 10 15

Ala Gly Gly Arg Arg Gln Arg Ser Gln Pro Gly Ser Ala Gln Gly Ser
 20 25 30

Gly Lys Arg Pro Pro Gln Lys Gln Phe Leu Gln Ile Val Pro Arg Gly
 35 40 45

Val Met Phe Asp Gly Gln Thr Gly Leu Ile Lys His Lys Thr Gly Arg
 50 55 60

Leu Pro Leu Met Phe Tyr Arg Glu Ile Lys His Leu Leu Ser His Asp
 65 70 75 80

Met Val Trp Pro Cys Pro Trp Arg Glu Thr Leu Val Gly Arg Val Val
 85 90 95
 Gly Pro Ile Arg Phe His Thr Tyr Asp Gln Thr Asp Ala Val Leu Phe
 100 105 110
 Phe Asp Ser Pro Glu Asn Val Ser Pro Arg Tyr Arg Gln His Leu Val
 115 120 125
 Pro Ser Gly Asn Val Leu Arg Phe Phe Gly Ala Thr Glu His Gly Tyr
 130 135 140
 Ser Ile Cys Val Asn Val Phe Gly Gln Arg Ser Tyr Phe Tyr Cys Glu
 145 150 155 160
 Tyr Ser Asp Thr Asp Arg Leu Arg Glu Val Ile Ala Ser Val Gly Glu
 165 170 175
 Leu Val Pro Glu Pro Arg Thr Pro Tyr Ala Val Ser Val Thr Pro Ala
 180 185 190
 Thr Lys Thr Ser Ile Tyr Gly Tyr Gly Thr Arg Pro Val Pro Asp Leu
 195 200 205
 Gln Cys Val Ser Ile Ser Asn Trp Thr Met Ala Arg Lys Ile Gly Glu
 210 215 220
 Tyr Leu Leu Glu Gln Gly Phe Pro Val Tyr Glu Val Arg Val Asp Pro
 225 230 235 240
 Leu Thr Arg Leu Val Ile Asp Arg Arg Ile Thr Thr Phe Gly Trp Cys
 245 250 255
 Ser Val Asn Arg Tyr Asp Trp Arg Gln Gln Gly Arg Ala Ser Thr Cys
 260 265 270
 Asp Ile Glu Val Asp Cys Asp Val Ser Asp Leu Val Ala Val Pro Asp
 275 280 285
 Asp Ser Ser Trp Pro Arg Tyr Arg Cys Leu Ser Phe Asp Ile Glu Cys
 290 295 300
 Met Ser Gly Glu Gly Gly Phe Pro Cys Ala Glu Lys Ser Asp Asp Ile
 305 310 315 320
 Val Ile Gln Ile Ser Cys Val Cys Tyr Glu Thr Gly Gly Asn Thr Ala
 325 330 335
 Val Asp Gln Gly Ile Pro Asn Gly Asn Asp Gly Arg Gly Cys Thr Ser
 340 345 350
 Glu Gly Val Ile Phe Gly His Ser Gly Leu His Leu Phe Thr Ile Gly
 355 360 365
 Thr Cys Gly Gln Val Gly Pro Asp Val Asp Val Tyr Glu Phe Pro Ser
 370 375 380
 Glu Tyr Glu Leu Leu Leu Gly Phe Met Leu Phe Phe Gln Arg Tyr Ala
 385 390 395 400
 Pro Ala Phe Val Thr Gly Tyr Asn Ile Asn Ser Phe Asp Leu Lys Tyr

405	410	415
Ile Leu Thr Arg Leu Glu Tyr Leu Tyr Lys Val Asp Ser Gln Arg Phe		
420	425	430
Cys Lys Leu Pro Thr Ala Gln Gly Gly Arg Phe Phe Leu His Ser Pro		
435	440	445
Ala Val Gly Phe Lys Arg Gln Tyr Ala Ala Ala Phe Pro Ser Ala Ser		
450	455	460
His Asn Asn Pro Ala Ser Thr Ala Ala Thr Lys Val Tyr Ile Ala Gly		
465	470	475
Ser Val Val Ile Asp Met Tyr Pro Val Cys Met Ala Lys Thr Asn Ser		
485	490	495
Pro Asn Tyr Lys Leu Asn Thr Met Ala Glu Leu Tyr Leu Arg Gln Arg		
500	505	510
Lys Asp Asp Leu Ser Tyr Lys Asp Ile Pro Arg Cys Phe Val Ala Asn		
515	520	525
Ala Glu Gly Arg Ala Gln Val Gly Arg Tyr Cys Leu Gln Asp Ala Val		
530	535	540
Leu Val Arg Asp Leu Phe Asn Thr Ile Asn Phe His Tyr Glu Ala Gly		
545	550	555
Ala Ile Ala Arg Leu Ala Lys Ile Pro Leu Arg Arg Val Ile Phe Asp		
565	570	575
Gly Gln Gln Ile Arg Ile Tyr Thr Ser Leu Leu Asp Glu Cys Ala Cys		
580	585	590
Arg Asp Phe Ile Leu Pro Asn His Tyr Ser Lys Gly Thr Thr Val Pro		
595	600	605
Glu Thr Asn Ser Val Ala Val Ser Pro Asn Ala Ala Ile Ile Ser Thr		
610	615	620
Ala Ala Val Pro Gly Asp Ala Gly Ser Val Ala Ala Met Phe Gln Met		
625	630	635
Ser Pro Pro Leu Gln Ser Ala Pro Ser Ser Gln Asp Gly Val Ser Pro		
645	650	655
Gly Ser Gly Ser Asn Ser Ser Ser Val Gly Val Phe Ser Val Gly		
660	665	670
Ser Gly Ser Ser Gly Gly Val Ser Asn Asp Asn His Gly Ala		
675	680	685
Gly Gly Thr Ala Ala Val Ser Tyr Gln Gly Ala Thr Val Phe Glu Pro		
690	695	700
Glu Val Gly Tyr Tyr Asn Asp Pro Val Ala Val Phe Asp Phe Ala Ser		
705	710	715
Leu Tyr Pro Ser Ile Ile Met Ala His Asn Leu Cys Tyr Ser Thr Leu		
725	730	735

Leu Val Pro Gly Gly Glu Tyr Pro Val Asp Pro Ala Asp Val Tyr Ser
 740 745 750
 Val Thr Leu Glu Asn Gly Val Thr His Arg Phe Val Arg Ala Ser Val
 755 760 765
 Arg Val Ser Val Leu Ser Glu Leu Leu Asn Lys Trp Val Ser Gln Arg
 770 775 780
 Arg Ala Val Arg Glu Cys Met Arg Glu Cys Gln Asp Pro Val Arg Arg
 785 790 795 800
 Met Leu Leu Asp Lys Glu Gln Met Ala Leu Lys Val Thr Cys Asn Ala
 805 810 815
 Phe Tyr Gly Phe Thr Gly Ala Leu Asn Gly Met Met Pro Cys Leu Pro
 820 825 830
 Ile Ala Ala Ser Ile Thr Arg Ile Gly Arg Asp Met Leu Glu Arg Thr
 835 840 845
 Ala Arg Phe Ile Lys Asp Asn Phe Ser Glu Pro Cys Phe Leu His Asn
 850 855 860
 Phe Phe Asn Gln Glu Asp Tyr Val Val Gly Thr Arg Glu Gly Asp Ser
 865 870 875 880
 Glu Glu Ser Ser Ala Leu Pro Glu Gly Leu Glu Thr Ser Ser Gly Gly
 885 890 895
 Ser Asn Glu Arg Arg Val Glu Ala Arg Val Ile Tyr Gly Asp Thr Asp
 900 905 910
 Ser Val Phe Val Arg Phe Arg Gly Leu Thr Pro Gln Ala Leu Val Ala
 915 920 925
 Arg Gly Pro Ser Leu Ala His Tyr Val Thr Ala Cys Leu Phe Val Glu
 930 935 940
 Pro Val Lys Leu Glu Phe Glu Lys Val Phe Val Ser Leu Met Met Ile
 945 950 955 960
 Cys Lys Lys Arg Tyr Ile Gly Lys Val Glu Gly Ala Ser Gly Leu Ser
 965 970 975
 Met Lys Gly Val Asp Leu Val Arg Lys Thr Ala Cys Glu Phe Val Lys
 980 985 990
 Gly Val Thr Arg Asp Val Leu Ser Leu Leu Phe Glu Asp Arg Glu Val
 995 1000 1005
 Ser Glu Ala Ala Val Arg Leu Ser Arg Leu Ser Leu Asp Glu Val
 1010 1015 1020
 Lys Lys Tyr Gly Val Pro Arg Gly Phe Trp Arg Ile Leu Arg Arg
 1025 1030 1035
 Leu Val Gln Ala Arg Asp Asp Leu Tyr Leu His Arg Val Arg Val
 1040 1045 1050
 Glu Asp Leu Val Leu Ser Ser Val Leu Ser Lys Asp Ile Ser Leu
 1055 1060 1065

Tyr Arg Gln Ser Asn Leu Pro His Ile Ala Val Ile Lys Arg Leu
 1070 1075 1080

Ala Ala Arg Ser Glu Glu Leu Pro Ser Val Gly Asp Arg Val Phe
 1085 1090 1095

Tyr Val Leu Thr Ala Pro Gly Val Arg Thr Ala Pro Gln Gly Ser
 1100 1105 1110

Ser Asp Asn Gly Asp Ser Val Thr Ala Gly Val Val Ser Arg Ser
 1115 1120 1125

Asp Ala Ile Asp Gly Thr Asp Asp Ala Asp Gly Gly Gly Val
 1130 1135 1140

Glu Glu Ser Asn Arg Arg Gly Gly Glu Pro Ala Lys Lys Arg Ala
 1145 1150 1155

Arg Lys Pro Pro Ser Ala Val Cys Asn Tyr Glu Val Ala Glu Asp
 1160 1165 1170

Pro Ser Tyr Val Arg Glu His Gly Val Pro Ile His Ala Asp Lys
 1175 1180 1185

Tyr Phe Glu Gln Val Leu Lys Ala Val Thr Asn Val Leu Ser Pro
 1190 1195 1200

Val Phe Pro Gly Gly Glu Thr Ala Arg Lys Asp Lys Phe Leu His
 1205 1210 1215

Met Val Leu Pro Arg Arg Leu His Leu Glu Pro Ala Phe Leu Pro
 1220 1225 1230

Tyr Ser Val Lys Ala His Glu Cys Cys
 1235 1240

<210> 13
 <211> 1242
 <212> PRT
 <213> herpes simplex

<400> 13

Met Phe Phe Asn Pro Tyr Leu Ser Gly Gly Val Thr Gly Ala Val
 1 5 10 15

Ala Gly Gly Arg Arg Gln Arg Ser Gln Pro Gly Ser Ala Gln Gly Ser
 20 25 30

Gly Lys Arg Pro Pro Gln Lys Gln Phe Leu Gln Ile Val Pro Arg Gly
 35 40 45

Val Met Phe Asp Gly Gln Thr Gly Leu Ile Lys His Lys Thr Gly Arg
 50 55 60

Leu Pro Leu Met Phe Tyr Arg Glu Ile Lys His Leu Leu Ser His Asp
 65 70 75 80

Met Val Trp Pro Cys Pro Trp Arg Glu Thr Leu Val Gly Arg Val Val
 85 90 95

Gly Pro Ile Arg Phe His Thr Tyr Asp Gln Thr Asp Ala Val Leu Phe
 100 105 110
 Phe Asp Ser Pro Glu Asn Val Ser Pro Arg Tyr Arg Gln His Leu Val
 115 120 125
 Pro Ser Gly Asn Val Leu Arg Phe Phe Gly Ala Thr Glu His Gly Tyr
 130 135 140
 Ser Ile Cys Val Asn Val Phe Gly Gln Arg Ser Tyr Phe Tyr Cys Glu
 145 150 155 160
 Tyr Ser Asp Thr Asp Arg Leu Arg Glu Val Ile Ala Ser Val Gly Glu
 165 170 175
 Leu Val Pro Glu Pro Arg Thr Pro Tyr Ala Val Ser Val Thr Pro Ala
 180 185 190
 Thr Lys Thr Ser Ile Tyr Gly Tyr Gly Thr Arg Pro Val Pro Asp Leu
 195 200 205
 Gln Cys Val Ser Ile Ser Asn Trp Thr Met Ala Arg Lys Ile Gly Glu
 210 215 220
 Tyr Leu Leu Glu Gln Gly Phe Pro Val Tyr Glu Val Arg Val Asp Pro
 225 230 235 240
 Leu Thr Arg Leu Val Ile Asp Arg Arg Ile Thr Thr Phe Gly Trp Cys
 245 250 255
 Ser Val Asn Arg Tyr Asp Trp Arg Gln Gln Gly Arg Ala Ser Thr Cys
 260 265 270
 Asp Ile Glu Val Asp Cys Asp Val Ser Asp Leu Val Ala Val Pro Asp
 275 280 285
 Asp Ser Ser Trp Pro Arg Tyr Arg Cys Leu Ser Phe Asp Ile Glu Cys
 290 295 300
 Met Ser Gly Glu Gly Phe Pro Cys Ala Glu Lys Ser Asp Asp Ile
 305 310 315 320
 Val Ile Gln Ile Ser Cys Val Cys Tyr Glu Thr Gly Gly Asn Thr Ala
 325 330 335
 Val Asp Gln Gly Ile Pro Asn Gly Asn Asp Gly Arg Gly Cys Thr Ser
 340 345 350
 Glu Gly Val Ile Phe Gly His Ser Gly Leu His Leu Phe Thr Ile Gly
 355 360 365
 Thr Cys Gly Gln Val Gly Pro Asp Val Asp Val Tyr Glu Phe Pro Ser
 370 375 380
 Glu Tyr Glu Leu Leu Leu Gly Phe Met Leu Phe Phe Gln Arg Tyr Ala
 385 390 395 400
 Pro Ala Phe Val Thr Gly Tyr Asn Ile Asn Ser Phe Asp Leu Lys Tyr
 405 410 415
 Ile Leu Thr Arg Leu Glu Tyr Leu Tyr Lys Val Asp Ser Gln Arg Phe
 420 425 430

Cys Lys Leu Pro Thr Ala Gln Gly Gly Arg Phe Phe Leu His Ser Pro
 435 440 445
 Ala Val Gly Phe Lys Arg Gln Tyr Ala Ala Ala Phe Pro Ser Ala Ser
 450 455 460
 His Asn Asn Pro Ala Ser Thr Ala Ala Thr Lys Val Tyr Ile Ala Gly
 465 470 475 480
 Ser Val Val Ile Asp Met Tyr Pro Val Cys Met Ala Lys Thr Asn Ser
 485 490 495
 Pro Asn Tyr Lys Leu Asn Thr Met Ala Glu Leu Tyr Leu Arg Gln Arg
 500 505 510
 Lys Asp Asp Leu Ser Tyr Lys Asp Ile Pro Arg Cys Phe Val Ala Asn
 515 520 525
 Ala Glu Gly Arg Ala Gln Val Gly Arg Tyr Cys Leu Gln Asp Ala Val
 530 535 540
 Leu Val Arg Asp Leu Phe Asn Thr Ile Asn Phe His Tyr Glu Ala Gly
 545 550 555 560
 Ala Ile Ala Arg Leu Ala Lys Ile Pro Leu Arg Arg Val Ile Phe Asp
 565 570 575
 Gly Gln Gln Ile Arg Ile Tyr Thr Ser Leu Leu Asp Glu Cys Ala Cys
 580 585 590
 Arg Asp Phe Ile Leu Pro Asn His Tyr Ser Lys Gly Thr Thr Val Pro
 595 600 605
 Glu Thr Asn Ser Val Ala Val Ser Pro Asn Ala Ile Ile Ser Thr
 610 615 620
 Ala Ala Val Pro Gly Asp Ala Gly Ser Val Ala Ala Met Phe Gln Met
 625 630 635 640
 Ser Pro Pro Leu Gln Ser Ala Pro Ser Ser Gln Asp Gly Val Ser Pro
 645 650 655
 Gly Ser Gly Ser Asn Ser Ser Ser Val Gly Val Phe Ser Val Gly
 660 665 670
 Ser Gly Ser Ser Gly Gly Val Gly Val Ser Asn Asp Asn His Gly Ala
 675 680 685
 Gly Gly Thr Ala Ala Val Ser Tyr Gln Gly Ala Thr Val Phe Glu Pro
 690 695 700
 Glu Val Gly Tyr Tyr Asn Asp Pro Val Ala Val Phe Asp Phe Ala Ser
 705 710 715 720
 Leu Tyr Pro Ser Ile Ile Met Ala His Asn Leu Cys Tyr Ser Thr Leu
 725 730 735
 Leu Val Pro Gly Gly Glu Tyr Pro Val Asp Pro Ala Asp Val Tyr Ser
 740 745 750
 Val Thr Leu Glu Asn Gly Val Thr His Arg Phe Val Arg Ala Ser Val

755	760	765
Arg Val Ser Val Leu Ser Glu Leu Leu Asn Lys Trp Val Ser Gln Arg		
770	775	780
Arg Ala Val Arg Glu Cys Met Arg Glu Cys Gln Asp Pro Val Arg Arg		
785	790	795
800		
Met Leu Leu Asp Lys Glu Gln Met Ala Leu Lys Val Thr Cys Asn Ala		
805	810	815
Phe Tyr Gly Phe Thr Gly Val Val Asn Gly Met Met Pro Cys Leu Pro		
820	825	830
Ile Ala Ala Ser Ile Thr Arg Ile Gly Arg Asp Met Leu Glu Arg Thr		
835	840	845
Ala Arg Phe Ile Lys Asp Asn Phe Ser Glu Pro Cys Phe Leu His Asn		
850	855	860
Phe Phe Asn Gln Glu Asp Tyr Val Val Gly Thr Arg Glu Gly Asp Ser		
865	870	875
880		
Glu Glu Ser Ser Ala Leu Pro Glu Gly Leu Glu Thr Ser Ser Gly Gly		
885	890	895
Ser Asn Glu Arg Arg Val Glu Ala Arg Val Ile Tyr Gly Asp Thr Asp		
900	905	910
Ser Val Phe Val Arg Phe Arg Gly Leu Thr Pro Gln Ala Leu Val Ala		
915	920	925
Arg Gly Pro Ser Leu Ala His Tyr Val Thr Ala Cys Leu Phe Val Glu		
930	935	940
Pro Val Lys Leu Glu Phe Glu Lys Val Phe Val Ser Leu Met Met Ile		
945	950	955
960		
Cys Lys Lys Arg Tyr Ile Gly Lys Val Glu Gly Ala Ser Gly Leu Ser		
965	970	975
Met Lys Gly Val Asp Leu Val Arg Lys Thr Ala Cys Glu Phe Val Lys		
980	985	990
Gly Val Thr Arg Asp Val Leu Ser Leu Leu Phe Glu Asp Arg Glu Val		
995	1000	1005
Ser Glu Ala Ala Val Arg Leu Ser Arg Leu Ser Leu Asp Glu Val		
1010	1015	1020
Lys Lys Tyr Gly Val Pro Arg Gly Phe Trp Arg Ile Leu Arg Arg		
1025	1030	1035
Leu Val Gln Ala Arg Asp Asp Leu Tyr Leu His Arg Val Arg Val		
1040	1045	1050
Glu Asp Leu Val Leu Ser Ser Val Leu Ser Lys Asp Ile Ser Leu		
1055	1060	1065
Tyr Arg Gln Ser Asn Leu Pro His Ile Ala Val Ile Lys Arg Leu		
1070	1075	1080

Ala Ala Arg Ser Glu Glu Leu Pro Ser Val Gly Asp Arg Val Phe
 1085 1090 1095

Tyr Val Leu Thr Ala Pro Gly Val Arg Thr Ala Pro Gln Gly Ser
 1100 1105 1110

Ser Asp Asn Gly Asp Ser Val Thr Ala Gly Val Val Ser Arg Ser
 1115 1120 1125

Asp Ala Ile Asp Gly Thr Asp Asp Ala Asp Gly Gly Gly Val
 1130 1135 1140

Glu Glu Ser Asn Arg Arg Gly Gly Glu Pro Ala Lys Lys Arg Ala
 1145 1150 1155

Arg Lys Pro Pro Ser Ala Val Cys Asn Tyr Glu Val Ala Glu Asp
 1160 1165 1170

Pro Ser Tyr Val Arg Glu His Gly Val Pro Ile His Ala Asp Lys
 1175 1180 1185

Tyr Phe Glu Gln Val Leu Lys Ala Val Thr Asn Val Leu Ser Pro
 1190 1195 1200

Val Phe Pro Gly Gly Glu Thr Ala Arg Lys Asp Lys Phe Leu His
 1205 1210 1215

Met Val Leu Pro Arg Arg Leu His Leu Glu Pro Ala Phe Leu Pro
 1220 1225 1230

Tyr Ser Val Lys Ala His Glu Cys Cys
 1235 1240

<210> 14
 <211> 1238
 <212> PRT
 <213> herpes simplex

<400> 14

Met Phe Cys Ala Ala Gly Gly Pro Thr Ser Pro Gly Gly Lys Ser Ala
 1 5 10 15

Ala Arg Ala Ala Ser Gly Phe Phe Ala Pro His Asn Pro Arg Gly Ala
 20 25 30

Thr Gln Thr Ala Pro Pro Cys Arg Arg Gln Asn Phe Tyr Asn Pro
 35 40 45

His Leu Ala Gln Thr Gly Thr Gln Pro Lys Ala Pro Gly Pro Ala Gln
 50 55 60

Arg His Thr Tyr Tyr Ser Glu Cys Asp Glu Phe Arg Phe Ile Ala Pro
 65 70 75 80

Arg Ser Leu Asp Glu Asp Ala Pro Ala Glu Gln Arg Thr Gly Val His
 85 90 95

Asp Gly Arg Leu Arg Arg Ala Pro Lys Val Tyr Cys Gly Gly Asp Glu
 100 105 110

Arg Asp Val Leu Arg Val Gly Pro Glu Gly Phe Trp Pro Arg Arg Leu

115	120	125
Arg Leu Trp Gly Gly Ala Asp His Ala Pro Lys Gly Phe Asp Pro Thr		
130	135	140
Val Thr Val Phe His Val Tyr Asp Ile Leu Glu His Val Glu His Ala		
145	150	155
160		
Tyr Ser Met Arg Ala Ala Gln Leu His Glu Arg Phe Met Asp Ala Ile		
165	170	175
Thr Pro Ala Gly Thr Val Ile Thr Leu Leu Gly Leu Thr Pro Glu Gly		
180	185	190
His Arg Val Ala Val His Val Tyr Gly Thr Arg Gln Tyr Phe Tyr Met		
195	200	205
Asn Lys Ala Glu Val Asp Arg His Leu Gln Cys Arg Ala Pro Arg Asp		
210	215	220
Leu Cys Glu Arg Leu Ala Ala Leu Arg Glu Ser Pro Gly Ala Ser		
225	230	235
240		
Phe Arg Gly Ile Ser Ala Asp His Phe Glu Ala Glu Val Val Glu Arg		
245	250	255
Ala Asp Val Tyr Tyr Tyr Glu Thr Arg Pro Thr Leu Tyr Tyr Arg Val		
260	265	270
Phe Val Arg Ser Gly Arg Ala Leu Ala Tyr Leu Cys Asp Asn Phe Cys		
275	280	285
Pro Ala Ile Arg Lys Tyr Glu Gly Gly Val Asp Ala Thr Thr Arg Phe		
290	295	300
Ile Leu Asp Asn Pro Gly Phe Val Thr Phe Gly Trp Tyr Arg Leu Lys		
305	310	315
320		
Pro Gly Arg Gly Asn Ala Pro Ala Gln Pro Arg Pro Pro Thr Ala Phe		
325	330	335
Gly Thr Ser Ser Asp Val Glu Phe Asn Cys Thr Ala Asp Asn Leu Ala		
340	345	350
Val Glu Gly Ala Met Cys Asp Leu Pro Ala Tyr Lys Leu Met Cys Phe		
355	360	365
Asp Ile Glu Cys Lys Ala Gly Gly Glu Asp Glu Leu Ala Phe Pro Val		
370	375	380
Ala Glu Arg Pro Glu Asp Leu Val Ile Gln Ile Ser Cys Leu Leu Tyr		
385	390	395
400		
Asp Leu Ser Thr Thr Ala Leu Glu His Ile Leu Leu Phe Ser Leu Gly		
405	410	415
Ser Cys Asp Leu Pro Glu Ser His Leu Ser Asp Leu Ala Ser Arg Gly		
420	425	430
Leu Pro Ala Pro Val Val Leu Glu Phe Asp Ser Glu Phe Glu Met Leu		
435	440	445

Leu Ala Phe Met Thr Phe Val Lys Gln Tyr Gly Pro Glu Phe Val Thr
 450 455 460
 Gly Tyr Asn Ile Ile Asn Phe Asp Trp Pro Phe Val Leu Thr Lys Leu
 465 470 475 480
 Thr Glu Ile Tyr Lys Val Pro Leu Asp Gly Tyr Gly Arg Met Asn Gly
 485 490 495
 Arg Gly Val Phe Arg Val Trp Asp Ile Gly Gln Ser His Phe Gln Lys
 500 505 510
 Arg Ser Lys Ile Lys Val Asn Gly Met Val Asn Ile Asp Met Tyr Gly
 515 520 525
 Ile Ile Thr Asp Lys Val Lys Leu Ser Ser Tyr Lys Leu Asn Ala Val
 530 535 540
 Ala Glu Ala Val Leu Lys Asp Lys Lys Asp Leu Ser Tyr Arg Asp
 545 550 555 560
 Ile Pro Ala Tyr Tyr Ala Ser Gly Pro Ala Gln Arg Gly Val Ile Gly
 565 570 575
 Glu Tyr Cys Val Gln Asp Ser Leu Leu Val Gly Gln Leu Phe Phe Lys
 580 585 590
 Phe Leu Pro His Leu Glu Leu Ser Ala Val Ala Arg Leu Ala Gly Ile
 595 600 605
 Asn Ile Thr Arg Thr Ile Tyr Asp Gly Gln Gln Ile Arg Val Phe Thr
 610 615 620
 Cys Leu Leu Arg Leu Ala Gly Gln Lys Gly Phe Ile Leu Pro Asp Thr
 625 630 635 640
 Gln Gly Arg Phe Arg Gly Leu Asp Lys Glu Ala Pro Lys Arg Pro Ala
 645 650 655
 Val Pro Arg Gly Glu Gly Glu Arg Pro Gly Asp Gly Asn Gly Asp Glu
 660 665 670
 Asp Lys Asp Asp Asp Glu Asp Glu Asp Gly Asp Glu Arg Glu Glu Val
 675 680 685
 Ala Arg Glu Thr Gly Gly Arg His Val Gly Tyr Gln Gly Ala Arg Val
 690 695 700
 Leu Asp Pro Thr Ser Gly Phe His Val Asp Pro Val Val Val Phe Asp
 705 710 715 720
 Phe Ala Ser Leu Tyr Pro Ser Ile Ile Gln Ala His Asn Leu Cys Phe
 725 730 735
 Ser Thr Leu Ser Leu Arg Pro Glu Ala Val Ala His Leu Glu Ala Asp
 740 745 750
 Arg Asp Tyr Leu Glu Ile Glu Val Gly Gly Arg Arg Leu Phe Phe Val
 755 760 765
 Lys Ala His Val Arg Glu Ser Leu Leu Ser Ile Leu Leu Arg Asp Trp
 770 775 780

Leu Ala Met Arg Lys Gln Ile Arg Ser Arg Ile Pro Gln Ser Thr Pro
 785 790 795 800
 Glu Glu Ala Val Leu Leu Asp Lys Gln Gln Ala Ala Ile Lys Val Val
 805 810 815
 Cys Asn Ser Val Tyr Gly Phe Thr Gly Val Gln His Gly Leu Leu Pro
 820 825 830
 Cys Leu His Val Ala Ala Thr Val Thr Thr Ile Gly Arg Glu Met Leu
 835 840 845
 Leu Ala Thr Arg Ala Tyr Val His Ala Arg Trp Ala Glu Phe Asp Gln
 850 855 860
 Leu Leu Ala Asp Phe Pro Glu Ala Ala Gly Met Arg Ala Pro Gly Pro
 865 870 875 880
 Tyr Ser Met Arg Ile Ile Tyr Gly Asp Thr Asp Ser Ile Phe Val Leu
 885 890 895
 Cys Arg Gly Leu Thr Ala Ala Gly Leu Val Ala Met Gly Asp Lys Met
 900 905 910
 Ala Ser His Ile Ser Arg Ala Leu Phe Leu Pro Pro Ile Lys Leu Glu
 915 920 925
 Cys Glu Lys Thr Phe Thr Lys Leu Leu Leu Ile Ala Lys Lys Lys Tyr
 930 935 940
 Ile Gly Val Ile Cys Gly Gly Lys Met Leu Ile Lys Gly Val Asp Leu
 945 950 955 960
 Val Arg Lys Asn Asn Cys Ala Phe Ile Asn Arg Thr Ser Arg Ala Leu
 965 970 975
 Val Asp Leu Leu Phe Tyr Asp Asp Thr Val Ser Gly Ala Ala Ala
 980 985 990
 Leu Ala Glu Arg Pro Ala Glu Glu Trp Leu Ala Arg Pro Leu Pro Glu
 995 1000 1005
 Gly Leu Gln Ala Phe Gly Ala Val Leu Val Asp Ala His Arg Arg
 1010 1015 1020
 Ile Thr Asp Pro Glu Arg Asp Ile Gln Asp Phe Val Leu Thr Ala
 1025 1030 1035
 Glu Leu Ser Arg His Pro Arg Ala Tyr Thr Asn Lys Arg Leu Ala
 1040 1045 1050
 His Leu Thr Val Tyr Tyr Lys Leu Met Ala Arg Arg Ala Gln Val
 1055 1060 1065
 Pro Ser Ile Lys Asp Arg Ile Pro Tyr Val Ile Val Ala Gln Thr
 1070 1075 1080
 Arg Glu Val Glu Glu Thr Val Ala Arg Leu Ala Ala Leu Arg Glu
 1085 1090 1095
 Leu Asp Ala Ala Ala Pro Gly Asp Glu Pro Ala Pro Pro Ala Ala

1100	1105	1110	
Leu Pro Ser Pro Ala Lys Arg Pro Arg Glu Thr Pro Ser His Ala			
1115	1120	1125	
Asp Pro Pro Gly Gly Ala Ser Lys Pro Arg Lys Leu Leu Val Ser			
1130	1135	1140	
Glu Leu Ala Glu Asp Pro Gly Tyr Ala Ile Ala Arg Gly Val Pro			
1145	1150	1155	
Leu Asn Thr Asp Tyr Tyr Phe Ser His Leu Leu Gly Ala Ala Cys			
1160	1165	1170	
Val Thr Phe Lys Ala Leu Phe Gly Asn Asn Ala Lys Ile Thr Glu			
1175	1180	1185	
Ser Leu Leu Lys Arg Phe Ile Pro Glu Thr Trp His Pro Pro Asp			
1190	1195	1200	
Asp Val Ala Ala Arg Leu Arg Ala Ala Gly Phe Gly Pro Ala Gly			
1205	1210	1215	
Ala Gly Ala Thr Ala Glu Glu Thr Arg Arg Met Leu His Arg Ala			
1220	1225	1230	
Phe Asp Thr Leu Ala			
1235			
<210> 15			
<211> 1240			
<212> PRT			
<213> herpes simplex			
<400> 15			
Met Phe Cys Ala Ala Gly Gly Pro Ala Ser Pro Gly Gly Lys Ser Ala			
1	5	10	15
Ala Arg Ala Ala Ser Gly Phe Phe Ala Pro His Asn Pro Arg Gly Ala			
20	25	30	
Thr Gln Thr Ala Pro Pro Pro Cys Arg Arg Gln Asn Phe Tyr Asn Pro			
35	40	45	
His Leu Ala Gln Thr Gly Thr Gln Pro Lys Ala Pro Gly Pro Ala Gln			
50	55	60	
Arg His Thr Tyr Tyr Ser Glu Cys Asp Glu Phe Arg Phe Ile Ala Pro			
65	70	75	80
Arg Ser Leu Asp Glu Asp Ala Pro Ala Glu Gln Arg Thr Gly Val His			
85	90	95	
Asp Gly Arg Leu Arg Arg Ala Pro Lys Val Tyr Cys Gly Gly Asp Glu			
100	105	110	
Arg Asp Val Leu Arg Val Gly Pro Glu Gly Phe Trp Pro Arg Arg Leu			
115	120	125	
Arg Leu Trp Gly Gly Ala Asp His Ala Pro Glu Gly Phe Asp Pro Thr			
130	135	140	

Val Thr Val Phe His Val Tyr Asp Ile Leu Glu His Val Glu His Ala
 145 150 155 160
 Tyr Ser Met Arg Ala Ala Gln Leu His Glu Arg Phe Met Asp Ala Ile
 165 170 175
 Thr Pro Ala Gly Thr Val Ile Thr Leu Leu Gly Leu Thr Pro Glu Gly
 180 185 190
 His Arg Val Ala Val His Val Tyr Gly Thr Arg Gln Tyr Phe Tyr Met
 195 200 205
 Asn Lys Ala Glu Val Asp Arg His Leu Gln Cys Arg Ala Pro Arg Asp
 210 215 220
 Leu Cys Glu Arg Leu Ala Ala Leu Arg Glu Ser Pro Gly Ala Ser
 225 230 235 240
 Phe Arg Gly Ile Ser Ala Asp His Phe Glu Ala Glu Val Val Glu Arg
 245 250 255
 Ala Asp Val Tyr Tyr Tyr Glu Thr Arg Pro Thr Leu Tyr Tyr Arg Val
 260 265 270
 Phe Val Arg Ser Gly Arg Ala Leu Ala Tyr Leu Cys Asp Asn Phe Cys
 275 280 285
 Pro Ala Ile Arg Lys Tyr Glu Gly Gly Val Asp Ala Thr Thr Arg Phe
 290 295 300
 Ile Leu Asp Asn Pro Gly Phe Val Thr Phe Gly Trp Tyr Arg Leu Lys
 305 310 315 320
 Pro Gly Arg Gly Asn Ala Pro Ala Gln Pro Arg Pro Pro Thr Ala Phe
 325 330 335
 Gly Thr Ser Ser Asp Val Glu Phe Asn Cys Thr Ala Asp Asn Leu Ala
 340 345 350
 Val Glu Gly Ala Met Cys Asp Leu Pro Ala Tyr Lys Leu Met Cys Phe
 355 360 365
 Asp Ile Glu Cys Lys Ala Gly Gly Glu Asp Glu Leu Ala Phe Pro Val
 370 375 380
 Ala Glu Arg Pro Glu Asp Leu Val Ile Gln Ile Ser Cys Leu Leu Tyr
 385 390 395 400
 Asp Leu Ser Thr Thr Ala Leu Glu His Ile Leu Leu Phe Ser Leu Gly
 405 410 415
 Ser Cys Asp Leu Pro Glu Ser His Leu Ser Asp Leu Ala Ser Arg Gly
 420 425 430
 Leu Pro Ala Pro Val Val Leu Glu Phe Asp Ser Glu Phe Glu Met Leu
 435 440 445
 Leu Ala Phe Met Thr Phe Val Lys Gln Tyr Gly Pro Glu Phe Val Thr
 450 455 460
 Gly Tyr Asn Ile Ile Asn Phe Asp Trp Pro Phe Val Leu Thr Lys Leu

465	470	475	480
Thr Glu Ile Tyr Lys Val Pro Leu Asp Gly Tyr Gly Arg Met Asn Gly			
485	490	495	
Arg Gly Val Phe Arg Val Trp Asp Ile Gly Gln Ser His Phe Gln Lys			
500	505	510	
Arg Ser Lys Ile Lys Val Asn Gly Met Val Asn Ile Asp Met Tyr Gly			
515	520	525	
Ile Ile Thr Asp Lys Val Lys Leu Ser Ser Tyr Lys Leu Asn Ala Val			
530	535	540	
Ala Glu Ala Val Leu Lys Asp Lys Lys Lys Asp Leu Ser Tyr Arg Asp			
545	550	555	560
Ile Pro Ala Tyr Tyr Ala Ser Gly Pro Ala Gln Arg Gly Val Ile Gly			
565	570	575	
Glu Tyr Cys Val Gln Asp Ser Leu Leu Val Gly Gln Leu Phe Phe Lys			
580	585	590	
Phe Leu Pro His Leu Glu Leu Ser Ala Val Ala Arg Leu Ala Gly Ile			
595	600	605	
Asn Ile Thr Arg Thr Ile Tyr Asp Gly Gln Gln Ile Arg Val Phe Thr			
610	615	620	
Cys Leu Leu Arg Leu Ala Gly Gln Lys Gly Phe Ile Leu Pro Asp Thr			
625	630	635	640
Gln Gly Arg Phe Arg Gly Leu Asp Lys Glu Ala Pro Lys Arg Pro Ala			
645	650	655	
Val Pro Arg Gly Glu Gly Glu Arg Pro Gly Asp Gly Asn Gly Asp Glu			
660	665	670	
Asp Lys Asp Asp Asp Glu Asp Gly Asp Glu Asp Gly Asp Glu Arg Glu			
675	680	685	
Glu Val Ala Arg Glu Thr Gly Gly Arg His Val Gly Tyr Gln Gly Ala			
690	695	700	
Arg Val Leu Asp Pro Thr Ser Gly Phe His Val Asp Pro Val Val Val			
705	710	715	720
Phe Asp Phe Ala Ser Leu Tyr Pro Ser Ile Ile Gln Ala His Asn Leu			
725	730	735	
Cys Phe Ser Thr Leu Ser Leu Arg Pro Glu Ala Val Ala His Leu Glu			
740	745	750	
Ala Asp Arg Asp Tyr Leu Glu Ile Glu Val Gly Gly Arg Arg Leu Phe			
755	760	765	
Phe Val Lys Ala His Val Arg Glu Ser Leu Leu Ser Ile Leu Leu Arg			
770	775	780	
Asp Trp Leu Ala Met Arg Lys Gln Ile Arg Ser Arg Ile Pro Gln Ser			
785	790	795	800

Pro Pro Glu Glu Ala Val Leu Leu Asp Lys Gln Gln Ala Ala Ile Lys
 805 810 815
 Val Val Cys Asn Ser Val Tyr Gly Phe Thr Gly Val Gln His Gly Leu
 820 825 830
 Leu Pro Cys Leu His Val Ala Ala Thr Val Thr Thr Ile Gly Arg Glu
 835 840 845
 Met Leu Leu Ala Thr Arg Ala Tyr Val His Ala Arg Trp Ala Glu Phe
 850 855 860
 Asp Gln Leu Leu Ala Asp Phe Pro Glu Ala Ala Gly Met Arg Ala Pro
 865 870 875 880
 Gly Pro Tyr Ser Met Arg Ile Ile Tyr Gly Asp Thr Asp Ser Ile Phe
 885 890 895
 Val Leu Cys Arg Gly Leu Thr Ala Ala Gly Leu Val Ala Met Gly Asp
 900 905 910
 Lys Met Ala Ser His Ile Ser Arg Ala Leu Phe Leu Pro Pro Ile Lys
 915 920 925
 Leu Glu Cys Glu Lys Thr Phe Thr Lys Leu Leu Leu Ile Ala Lys Lys
 930 935 940
 Lys Tyr Ile Gly Val Ile Cys Gly Gly Lys Met Leu Ile Lys Gly Val
 945 950 955 960
 Asp Leu Val Arg Lys Asn Asn Cys Ala Phe Ile Asn Arg Thr Ser Arg
 965 970 975
 Ala Leu Val Asp Leu Leu Phe Tyr Asp Asp Thr Val Ser Gly Ala Ala
 980 985 990
 Ala Ala Leu Ala Glu Arg Pro Ala Glu Glu Trp Leu Ala Arg Pro Leu
 995 1000 1005
 Pro Glu Gly Leu Gln Ala Phe Gly Ala Val Leu Val Asp Ala His
 1010 1015 1020
 Arg Arg Ile Thr Asp Pro Glu Arg Asp Ile Gln Asp Phe Val Leu
 1025 1030 1035
 Thr Ala Glu Leu Ser Arg His Pro Arg Ala Tyr Thr Asn Lys Arg
 1040 1045 1050
 Leu Ala His Leu Thr Val Tyr Tyr Lys Leu Met Ala Arg Arg Ala
 1055 1060 1065
 Gln Val Pro Ser Ile Lys Asp Arg Ile Pro Tyr Val Ile Val Ala
 1070 1075 1080
 Gln Thr Arg Glu Val Glu Glu Thr Val Ala Arg Leu Ala Ala Leu
 1085 1090 1095
 Arg Glu Leu Asp Ala Ala Pro Gly Asp Glu Pro Ala Pro Pro
 1100 1105 1110
 Ala Ala Leu Pro Ser Pro Ala Lys Arg Pro Arg Glu Thr Pro Ser
 1115 1120 1125

His Ala Asp Pro Pro Gly Gly Ala Ser Lys Pro Arg Lys Leu Leu
 1130 1135 1140

Val Ser Glu Leu Ala Glu Asp Pro Gly Tyr Ala Ile Ala Arg Gly
 1145 1150 1155

Val Pro Leu Asn Thr Asp Tyr Tyr Phe Ser His Leu Leu Gly Ala
 1160 1165 1170

Ala Cys Val Thr Phe Lys Ala Leu Phe Gly Asn Asn Ala Lys Ile
 1175 1180 1185

Thr Glu Ser Leu Leu Lys Arg Phe Ile Pro Glu Thr Trp His Pro
 1190 1195 1200

Pro Asp Asp Val Ala Ala Arg Leu Arg Ala Ala Gly Phe Gly Pro
 1205 1210 1215

Ala Gly Ala Gly Ala Thr Ala Glu Glu Thr Arg Arg Met Leu His
 1220 1225 1230

Arg Ala Phe Asp Thr Leu Ala
 1235 1240

<210> 16

<211> 1235

<212> PRT

<213> herpes simplex

<400> 16

Met Phe Ser Gly Gly Gly Pro Leu Ser Pro Gly Gly Lys Ser Ala
 1 5 10 15

Ala Arg Ala Ala Ser Gly Phe Phe Ala Pro Ala Gly Pro Arg Gly Ala
 20 25 30

Gly Arg Gly Pro Pro Pro Cys Leu Arg Gln Asn Phe Tyr Asn Pro Tyr
 35 40 45

Leu Ala Pro Val Gly Thr Gln Gln Lys Pro Thr Gly Pro Thr Gln Arg
 50 55 60

His Thr Tyr Tyr Ser Glu Cys Asp Glu Phe Arg Phe Ile Ala Pro Arg
 65 70 75 80

Val Leu Asp Glu Asp Ala Pro Pro Glu Lys Arg Ala Gly Val His Asp
 85 90 95

Gly His Leu Lys Arg Ala Pro Lys Val Tyr Cys Gly Gly Asp Glu Arg
 100 105 110

Asp Val Leu Arg Val Gly Ser Gly Gly Phe Trp Pro Arg Arg Ser Arg
 115 120 125

Leu Trp Gly Gly Val Asp His Ala Pro Ala Gly Phe Asn Pro Thr Val
 130 135 140

Thr Val Phe His Val Tyr Asp Ile Leu Glu Asn Val Glu His Ala Tyr
 145 150 155 160

Gly Met Arg Ala Ala Gln Phe His Ala Arg Phe Met Asp Ala Ile Thr
 165 170 175
 Pro Thr Gly Thr Val Ile Thr Leu Leu Gly Leu Thr Pro Glu Gly His
 180 185 190
 Arg Val Ala Val His Val Tyr Gly Thr Arg Gln Tyr Phe Tyr Met Asn
 195 200 205
 Lys Glu Glu Val Asp Arg His Leu Gln Cys Arg Ala Pro Arg Asp Leu
 210 215 220
 Cys Glu Arg Met Ala Ala Leu Arg Glu Ser Pro Gly Ala Ser Phe
 225 230 235 240
 Arg Gly Ile Ser Ala Asp His Phe Glu Ala Glu Val Val Glu Arg Thr
 245 250 255
 Asp Val Tyr Tyr Tyr Glu Thr Arg Pro Ala Leu Phe Tyr Arg Val Tyr
 260 265 270
 Val Arg Ser Gly Arg Val Leu Ser Tyr Leu Cys Asp Asn Phe Cys Pro
 275 280 285
 Ala Ile Lys Lys Tyr Glu Gly Val Asp Ala Thr Thr Arg Phe Ile
 290 295 300
 Leu Asp Asn Pro Gly Phe Val Thr Phe Gly Trp Tyr Arg Leu Lys Pro
 305 310 315 320
 Gly Arg Asn Asn Thr Leu Ala Gln Pro Arg Ala Pro Met Ala Phe Gly
 325 330 335
 Thr Ser Ser Asp Val Glu Phe Asn Cys Thr Ala Asp Asn Leu Ala Ile
 340 345 350
 Glu Gly Gly Met Ser Asp Leu Pro Ala Tyr Lys Leu Met Cys Phe Asp
 355 360 365
 Ile Glu Cys Lys Ala Gly Gly Glu Asp Glu Leu Ala Phe Pro Val Ala
 370 375 380
 Gly His Pro Glu Asp Leu Val Ile Gln Ile Ser Cys Leu Leu Tyr Asp
 385 390 395 400
 Leu Ser Thr Thr Ala Leu Glu His Val Leu Leu Phe Ser Leu Gly Ser
 405 410 415
 Cys Asp Leu Pro Glu Ser His Leu Asn Glu Leu Ala Ala Arg Gly Leu
 420 425 430
 Pro Thr Pro Val Val Leu Glu Phe Asp Ser Glu Phe Glu Met Leu Leu
 435 440 445
 Ala Phe Met Thr Leu Val Lys Gln Tyr Gly Pro Glu Phe Val Thr Gly
 450 455 460
 Tyr Asn Ile Ile Asn Phe Asp Trp Pro Phe Leu Leu Ala Lys Leu Thr
 465 470 475 480
 Asp Ile Tyr Lys Val Pro Leu Asp Gly Tyr Gly Arg Met Asn Gly Arg
 485 490 495

Gly Val Phe Arg Val Trp Asp Ile Gly Gln Ser His Phe Gln Lys Arg
 500 505 510
 Ser Lys Ile Lys Val Asn Gly Met Val Asn Ile Asp Met Tyr Gly Ile
 515 520 525
 Ile Thr Asp Lys Ile Lys Leu Ser Ser Tyr Lys Leu Asn Ala Val Ala
 530 535 540
 Glu Ala Val Leu Lys Asp Lys Lys Asp Leu Ser Tyr Arg Asp Ile
 545 550 555 560
 Pro Ala Tyr Tyr Ala Ala Gly Pro Ala Gln Arg Gly Val Ile Gly Glu
 565 570 575
 Tyr Cys Ile Gln Asp Ser Leu Leu Val Gly Gln Leu Phe Phe Lys Phe
 580 585 590
 Leu Pro His Leu Glu Leu Ser Ala Val Ala Arg Leu Ala Gly Ile Asn
 595 600 605
 Ile Thr Arg Thr Ile Tyr Asp Gly Gln Gln Ile Arg Val Phe Thr Cys
 610 615 620
 Leu Leu Arg Leu Ala Asp Gln Lys Gly Phe Ile Leu Pro Asp Thr Gln
 625 630 635 640
 Gly Arg Phe Arg Gly Ala Gly Glu Ala Pro Lys Arg Pro Ala Ala
 645 650 655
 Ala Arg Glu Asp Glu Glu Arg Pro Glu Glu Gly Glu Asp Glu Asp
 660 665 670
 Glu Arg Glu Glu Gly Gly Glu Arg Glu Pro Glu Gly Ala Arg Glu
 675 680 685
 Thr Ala Gly Arg His Val Gly Tyr Gln Gly Ala Arg Val Leu Asp Pro
 690 695 700
 Thr Ser Gly Phe His Val Asn Pro Val Val Phe Asp Phe Ala Ser
 705 710 715 720
 Leu Tyr Pro Ser Ile Ile Gln Ala His Asn Leu Cys Phe Ser Thr Leu
 725 730 735
 Ser Leu Arg Ala Asp Ala Val Ala His Leu Glu Ala Gly Lys Asp Tyr
 740 745 750
 Leu Glu Ile Glu Val Gly Gly Arg Arg Leu Phe Phe Val Lys Ala His
 755 760 765
 Val Arg Glu Ser Leu Leu Ser Ile Leu Leu Arg Asp Trp Leu Ala Met
 770 775 780
 Arg Lys Gln Ile Arg Ser Arg Ile Pro Gln Ser Ser Pro Glu Glu Ala
 785 790 795 800
 Val Leu Leu Asp Lys Gln Gln Ala Ala Ile Lys Val Val Cys Asn Ser
 805 810 815
 Val Tyr Gly Phe Thr Gly Val Gln His Gly Leu Leu Pro Cys Leu His

820	825	830
Val Ala Ala Thr Val Thr Thr Ile Gly Arg Glu Met Leu Leu Ala Thr		
835	840	845
Arg Glu Tyr Val His Ala Arg Trp Ala Ala Phe Glu Gln Leu Leu Ala		
850	855	860
Asp Phe Pro Glu Ala Ala Asp Met Arg Ala Pro Gly Pro Tyr Ser Met		
865	870	875
Arg Ile Ile Tyr Gly Asp Thr Asp Ser Ile Phe Val Leu Cys Arg Gly		
885	890	895
Leu Thr Ala Ala Gly Leu Thr Ala Met Gly Asp Lys Met Ala Ser His		
900	905	910
Ile Ser Arg Ala Leu Phe Leu Pro Pro Ile Lys Leu Glu Cys Glu Lys		
915	920	925
Thr Phe Thr Lys Leu Leu Ile Ala Lys Lys Tyr Ile Gly Val		
930	935	940
Ile Tyr Gly Gly Lys Met Leu Ile Lys Gly Val Asp Leu Val Arg Lys		
945	950	955
Asn Asn Cys Ala Phe Ile Asn Arg Thr Ser Arg Ala Leu Val Asp Leu		
965	970	975
Leu Phe Tyr Asp Asp Thr Val Ser Gly Ala Ala Ala Leu Ala Glu		
980	985	990
Arg Pro Ala Glu Glu Trp Leu Ala Arg Pro Leu Pro Glu Gly Leu Gln		
995	1000	1005
Ala Phe Gly Ala Val Leu Val Asp Ala His Arg Arg Ile Thr Asp		
1010	1015	1020
Pro Glu Arg Asp Ile Gln Asp Phe Val Leu Thr Ala Glu Leu Ser		
1025	1030	1035
Arg His Pro Arg Ala Tyr Thr Asn Lys Arg Leu Ala His Leu Thr		
1040	1045	1050
Val Tyr Tyr Lys Leu Met Ala Arg Arg Ala Gln Val Pro Ser Ile		
1055	1060	1065
Lys Asp Arg Ile Pro Tyr Val Ile Val Ala Gln Thr Arg Glu Val		
1070	1075	1080
Glu Glu Thr Val Ala Arg Leu Ala Ala Leu Arg Glu Leu Asp Ala		
1085	1090	1095
Ala Ala Pro Gly Asp Glu Pro Ala Pro Pro Ala Ala Leu Pro Ser		
1100	1105	1110
Pro Ala Lys Arg Pro Arg Glu Thr Pro Ser His Ala Asp Pro Pro		
1115	1120	1125
Gly Gly Ala Ser Lys Pro Arg Lys Leu Leu Val Ser Glu Leu Ala		
1130	1135	1140

Glu Asp Pro Ala Tyr Ala Ile Ala His Gly Val Ala Leu Asn Thr
 1145 1150 1155
 Asp Tyr Tyr Phe Ser His Leu Leu Gly Ala Ala Cys Val Thr Phe
 1160 1165 1170
 Lys Ala Leu Phe Gly Asn Asn Ala Lys Ile Thr Glu Ser Leu Leu
 1175 1180 1185
 Lys Arg Phe Ile Pro Glu Val Trp His Pro Pro Asp Asp Val Ala
 1190 1195 1200
 Ala Arg Leu Arg Ala Ala Gly Phe Gly Ala Val Gly Ala Gly Ala
 1205 1210 1215
 Thr Ala Glu Glu Thr Arg Arg Met Leu His Arg Ala Phe Asp Thr
 1220 1225 1230
 Leu Ala
 1235
 <210> 17
 <211> 1235
 <212> PRT
 <213> herpes simplex
 <400> 17
 Met Phe Ser Gly Gly Gly Pro Leu Ser Pro Gly Gly Lys Ser Ala
 1 5 10 15
 Ala Arg Ala Ala Ser Gly Phe Phe Ala Pro Ala Gly Pro Arg Gly Ala
 20 25 30
 Gly Arg Gly Pro Pro Pro Cys Leu Arg Gln Asn Phe Tyr Asn Pro Tyr
 35 40 45
 Leu Ala Pro Val Gly Thr Gln Gln Lys Pro Thr Gly Pro Thr Gln Arg
 50 55 60
 His Thr Tyr Tyr Ser Glu Cys Asp Glu Phe Arg Phe Ile Ala Pro Arg
 65 70 75 80
 Val Leu Asp Glu Asp Ala Pro Pro Glu Lys Arg Ala Gly Val His Asp
 85 90 95
 Gly His Leu Lys Arg Ala Pro Lys Val Tyr Cys Gly Gly Asp Glu Arg
 100 105 110
 Asp Val Leu Arg Val Gly Ser Gly Gly Phe Trp Pro Arg Arg Ser Arg
 115 120 125
 Leu Trp Gly Gly Val Asp His Ala Pro Ala Gly Phe Asn Pro Thr Val
 130 135 140
 Thr Val Phe His Val Tyr Asp Ile Leu Glu Asn Val Glu His Ala Tyr
 145 150 155 160
 Gly Met Arg Ala Ala Gln Phe His Ala Arg Phe Met Asp Ala Ile Thr
 165 170 175
 Pro Thr Gly Thr Val Ile Thr Leu Leu Gly Leu Thr Pro Glu Gly His

180	185	190
Arg Val Ala Val His Val Tyr Gly Thr Arg Gln Tyr Phe Tyr Met Asn		
195	200	205
Lys Glu Glu Val Asp Arg His Leu Gln Cys Arg Ala Pro Arg Asp Leu		
210	215	220
Cys Glu Arg Met Ala Ala Ala Leu Arg Glu Ser Pro Gly Ala Ser Phe		
225	230	235
Arg Gly Ile Ser Ala Asp His Phe Glu Ala Glu Val Val Glu Arg Thr		
245	250	255
Asp Val Tyr Tyr Glu Thr Arg Pro Ala Leu Phe Tyr Arg Val Tyr		
260	265	270
Val Arg Ser Gly Arg Val Leu Ser Tyr Leu Cys Asp Asn Phe Cys Pro		
275	280	285
Ala Ile Lys Lys Tyr Glu Gly Gly Val Asp Ala Thr Thr Arg Phe Ile		
290	295	300
Leu Asp Asn Pro Gly Phe Val Thr Phe Gly Trp Tyr Arg Leu Lys Pro		
305	310	315
Gly Arg Asn Asn Thr Leu Ala Gln Pro Arg Ala Pro Met Ala Phe Gly		
325	330	335
Thr Ser Ser Asp Val Glu Phe Asn Cys Thr Ala Asp Asn Leu Ala Ile		
340	345	350
Glu Gly Gly Met Ser Asp Leu Pro Ala Tyr Lys Leu Met Cys Phe Asp		
355	360	365
Ile Glu Cys Lys Ala Gly Glu Asp Glu Leu Ala Phe Pro Val Ala		
370	375	380
Gly His Pro Glu Asp Leu Val Ile Gln Ile Ser Cys Leu Leu Tyr Asp		
385	390	395
Leu Ser Thr Thr Ala Leu Glu His Val Leu Leu Phe Ser Leu Gly Ser		
405	410	415
Cys Asp Leu Pro Glu Ser His Leu Asn Glu Leu Ala Ala Arg Gly Leu		
420	425	430
Pro Thr Pro Val Val Leu Glu Phe Asp Ser Glu Phe Glu Met Leu Leu		
435	440	445
Ala Phe Met Thr Leu Val Lys Gln Tyr Gly Pro Glu Phe Val Thr Gly		
450	455	460
Tyr Asn Ile Ile Asn Phe Asp Trp Pro Phe Leu Leu Ala Lys Leu Thr		
465	470	475
Asp Ile Tyr Lys Val Pro Leu Asp Gly Tyr Gly Arg Met Asn Gly Arg		
485	490	495
Gly Val Phe Arg Val Trp Asp Ile Gly Gln Ser His Phe Gln Lys Arg		
500	505	510

Ser Lys Ile Lys Val Asn Gly Met Val Asn Ile Asp Met Tyr Gly Ile
 515 520 525
 Ile Thr Asp Lys Ile Lys Leu Ser Ser Tyr Lys Leu Asn Ala Val Ala
 530 535 540
 Glu Ala Val Leu Lys Asp Lys Lys Asp Leu Ser Tyr Arg Asp Ile
 545 550 555 560
 Pro Ala Tyr Tyr Ala Ala Gly Pro Ala Gln Arg Gly Val Ile Gly Glu
 565 570 575
 Tyr Cys Ile Gln Asp Ser Leu Leu Val Gly Gln Leu Phe Phe Lys Phe
 580 585 590
 Leu Pro His Leu Glu Leu Ser Ala Val Ala Arg Leu Ala Gly Ile Asn
 595 600 605
 Ile Thr Arg Thr Ile Tyr Asp Gly Gln Gln Ile Arg Val Phe Thr Cys
 610 615 620
 Leu Leu Arg Leu Ala Asp Gln Lys Gly Phe Ile Leu Pro Asp Thr Gln
 625 630 635 640
 Gly Arg Phe Arg Gly Ala Gly Glu Ala Pro Lys Arg Pro Ala Ala
 645 650 655
 Ala Arg Glu Asp Glu Glu Arg Pro Glu Glu Gly Glu Asp Glu Asp
 660 665 670
 Glu Arg Glu Glu Gly Gly Glu Arg Glu Pro Glu Gly Ala Arg Glu
 675 680 685
 Thr Ala Gly Arg His Val Gly Tyr Gln Gly Ala Arg Val Leu Asp Pro
 690 695 700
 Ile Ser Gly Phe His Val Asn Pro Val Val Phe Asp Phe Ala Ser
 705 710 715 720
 Leu Tyr Pro Ser Ile Ile Gln Ala His Asn Leu Cys Phe Ser Thr Leu
 725 730 735
 Ser Leu Arg Ala Asp Ala Val Ala His Leu Glu Ala Gly Lys Asp Tyr
 740 745 750
 Leu Glu Ile Glu Val Gly Gly Arg Arg Leu Phe Phe Val Lys Ala His
 755 760 765
 Val Arg Glu Ser Leu Leu Ser Ile Leu Leu Arg Asp Trp Leu Ala Met
 770 775 780
 Arg Lys Gln Ile Arg Ser Arg Ile Pro Gln Ser Ser Pro Glu Glu Ala
 785 790 795 800
 Val Leu Leu Asp Lys Gln Gln Ala Ala Ile Lys Val Val Cys Asn Ser
 805 810 815
 Val Tyr Gly Phe Thr Gly Val Gln His Gly Leu Leu Pro Cys Leu His
 820 825 830
 Val Ala Ala Thr Val Thr Ile Gly Arg Glu Met Leu Leu Ala Thr
 835 840 845

Arg Glu Tyr Val His Ala Arg Trp Ala Ala Phe Glu Gln Leu Leu Ala
 850 855 860
 Asp Phe Pro Glu Ala Ala Asp Met Arg Ala Pro Gly Pro Tyr Ser Met
 865 870 875 880
 Arg Ile Ile Tyr Gly Asp Thr Asp Ser Ile Phe Val Leu Cys Arg Gly
 885 890 895
 Leu Thr Ala Ala Gly Leu Thr Ala Met Gly Asp Lys Met Ala Ser His
 900 905 910
 Ile Ser Arg Ala Leu Phe Leu Pro Pro Ile Lys Leu Glu Cys Glu Lys
 915 920 925
 Thr Phe Thr Lys Leu Leu Ile Ala Lys Lys Lys Tyr Ile Gly Val
 930 935 940
 Ile Tyr Gly Gly Lys Met Leu Ile Lys Gly Val Asp Leu Val Arg Lys
 945 950 955 960
 Asn Asn Cys Ala Phe Ile Asn Arg Thr Ser Arg Ala Leu Val Asp Leu
 965 970 975
 Leu Phe Tyr Asp Asp Thr Val Ser Gly Ala Ala Ala Leu Ala Glu
 980 985 990
 Arg Pro Ala Glu Glu Trp Leu Ala Arg Pro Leu Pro Glu Gly Leu Gln
 995 1000 1005
 Ala Phe Gly Ala Val Leu Val Asp Ala His Arg Arg Ile Thr Asp
 1010 1015 1020
 Pro Glu Arg Asp Ile Gln Asp Phe Val Leu Thr Ala Glu Leu Ser
 1025 1030 1035
 Arg His Pro Arg Ala Tyr Thr Asn Lys Arg Leu Ala His Leu Thr
 1040 1045 1050
 Val Tyr Tyr Lys Leu Met Ala Arg Arg Ala Gln Val Pro Ser Ile
 1055 1060 1065
 Lys Asp Arg Ile Pro Tyr Val Ile Val Ala Gln Thr Arg Glu Val
 1070 1075 1080
 Glu Glu Thr Val Ala Arg Leu Ala Ala Leu Arg Glu Leu Asp Ala
 1085 1090 1095
 Ala Ala Pro Gly Asp Glu Pro Ala Pro Pro Ala Ala Leu Pro Ser
 1100 1105 1110
 Pro Ala Lys Arg Pro Arg Glu Thr Pro Ser Pro Ala Asp Pro Pro
 1115 1120 1125
 Gly Gly Ala Ser Lys Pro Arg Lys Leu Leu Val Ser Glu Leu Ala
 1130 1135 1140
 Glu Asp Pro Ala Tyr Ala Ile Ala His Gly Val Ala Leu Asn Thr
 1145 1150 1155
 Asp Tyr Tyr Phe Ser His Leu Leu Gly Ala Ala Cys Val Thr Phe

1160	1165	1170
Lys Ala Leu Phe Gly Asn Asn Ala Lys Ile Thr Glu Ser Leu Leu		
1175	1180	1185
Lys Arg Phe Ile Pro Glu Val Trp His Pro Pro Asp Asp Val Thr		
1190	1195	1200
Ala Arg Leu Arg Ala Ala Gly Phe Gly Ala Val Gly Ala Gly Ala		
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Thr Ala Glu Glu Thr Arg Arg Met Leu His Arg Ala Phe Asp Thr		
1220	1225	1230
Leu Ala		
1235		
<210> 18		
<211> 1235		
<212> PRT		
<213> herpes simplex		
<400> 18		
Met Phe Ser Gly Gly Gly Pro Leu Ser Pro Gly Gly Lys Ser Ala		
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		15
Ala Arg Ala Ala Ser Gly Phe Phe Ala Pro Ala Gly Pro Arg Gly Ala		
20	25	30
Gly Arg Gly Pro Pro Pro Cys Leu Arg Gln Asn Phe Tyr Asn Pro Tyr		
35	40	45
Leu Ala Pro Val Gly Thr Gln Gln Lys Pro Thr Gly Pro Thr Gln Arg		
50	55	60
His Thr Tyr Tyr Ser Glu Cys Asp Glu Phe Arg Phe Ile Ala Pro Arg		
65	70	75
		80
Val Leu Asp Glu Asp Ala Pro Pro Glu Lys Arg Ala Gly Val His Asp		
85	90	95
Gly His Leu Lys Arg Ala Pro Lys Val Tyr Cys Gly Gly Asp Glu Arg		
100	105	110
Asp Val Leu Arg Val Gly Ser Gly Gly Phe Trp Pro Arg Arg Ser Arg		
115	120	125
Leu Trp Gly Gly Val Asp His Ala Pro Ala Gly Phe Asn Pro Thr Val		
130	135	140
Thr Val Phe His Val Tyr Asp Ile Leu Glu Asn Val Glu His Ala Tyr		
145	150	155
		160
Gly Met Arg Ala Ala Gln Phe His Ala Arg Phe Met Asp Ala Ile Thr		
165	170	175
Pro Thr Gly Thr Val Ile Thr Leu Leu Gly Leu Thr Pro Glu Gly His		
180	185	190
Arg Val Ala Val His Val Tyr Gly Thr Arg Gln Tyr Phe Tyr Met Asn		
195	200	205

Lys Glu Glu Val Asp Arg His Leu Gln Cys Arg Ala Pro Arg Asp Leu
 210 215 220

Cys Glu Arg Met Ala Ala Ala Leu Arg Glu Ser Pro Gly Ala Ser Phe
 225 230 235 240

Arg Gly Ile Ser Ala Asp His Phe Glu Ala Glu Val Val Glu Arg Thr
 245 250 255

Asp Val Tyr Tyr Tyr Glu Thr Arg Pro Ala Leu Phe Tyr Arg Val Tyr
 260 265 270

Val Arg Ser Gly Arg Val Leu Ser Tyr Leu Cys Asp Asn Phe Cys Pro
 275 280 285

Ala Ile Lys Lys Tyr Glu Gly Gly Val Asp Ala Thr Thr Arg Phe Ile
 290 295 300

Leu Asp Asn Pro Gly Phe Val Thr Phe Gly Trp Tyr Arg Leu Lys Pro
 305 310 315 320

Gly Arg Asn Asn Thr Leu Ala Gln Pro Arg Ala Pro Met Ala Phe Gly
 325 330 335

Thr Ser Ser Asp Val Glu Phe Asn Cys Thr Ala Asp Asn Leu Ala Ile
 340 345 350

Glu Gly Gly Met Ser Asp Leu Pro Ala Tyr Lys Leu Met Cys Phe Asp
 355 360 365

Ile Glu Cys Lys Ala Gly Gly Glu Asp Glu Leu Ala Phe Pro Val Ala
 370 375 380

Gly His Pro Glu Asp Leu Val Ile Gln Ile Ser Cys Leu Leu Tyr Asp
 385 390 395 400

Leu Ser Thr Thr Ala Leu Glu His Val Leu Leu Phe Ser Leu Gly Ser
 405 410 415

Cys Asp Leu Pro Glu Ser His Leu Asn Glu Leu Ala Ala Arg Gly Leu
 420 425 430

Pro Thr Pro Val Val Leu Glu Phe Asp Ser Glu Phe Glu Met Leu Leu
 435 440 445

Ala Phe Met Thr Leu Val Lys Gln Tyr Gly Pro Glu Phe Val Thr Gly
 450 455 460

Tyr Asn Ile Ile Asn Phe Asp Trp Pro Phe Leu Leu Ala Lys Leu Thr
 465 470 475 480

Asp Ile Tyr Lys Val Pro Leu Asp Gly Tyr Gly Arg Met Asn Gly Arg
 485 490 495

Gly Val Phe Arg Val Trp Asp Ile Gly Gln Ser His Phe Gln Lys Arg
 500 505 510

Ser Lys Ile Lys Val Asn Gly Met Val Asn Ile Asp Met Tyr Gly Ile
 515 520 525

Ile Thr Asp Lys Ile Lys Leu Ser Ser Tyr Lys Leu Asn Ala Val Ala

530	535	540
Glu Ala Val Leu Lys Asp Lys Lys Lys Asp Leu Ser Tyr Arg Asp Ile		
545	550	555
560		
Pro Thr Tyr Tyr Ala Ala Gly Pro Ala Gln Arg Gly Val Ile Gly Glu		
565	570	575
Tyr Cys Ile Gln Asp Ser Leu Leu Val Gly Gln Leu Phe Phe Lys Phe		
580	585	590
Leu Pro His Leu Glu Leu Ser Ala Val Ala Arg Leu Ala Gly Ile Asn		
595	600	605
Ile Thr Arg Thr Ile Tyr Asp Gly Gln Gln Ile Arg Val Phe Thr Cys		
610	615	620
Leu Leu Arg Leu Ala Asp Gln Lys Gly Phe Ile Leu Pro Asp Thr Gln		
625	630	635
640		
Gly Arg Phe Arg Gly Ala Gly Glu Ala Pro Lys Arg Pro Ala Ala		
645	650	655
Ala Arg Glu Asp Glu Glu Arg Pro Glu Glu Gly Glu Asp Glu Asn		
660	665	670
Glu Arg Glu Glu Gly Gly Glu Arg Glu Pro Glu Gly Ala Arg Glu		
675	680	685
Thr Ala Gly Arg His Val Gly Tyr Gln Gly Ala Arg Val Leu Asp Pro		
690	695	700
Thr Ser Gly Phe His Val Asn Pro Val Val Val Phe Asp Phe Ala Ser		
705	710	715
720		
Leu Tyr Pro Ser Ile Ile Gln Ala His Asn Leu Cys Phe Ser Thr Leu		
725	730	735
Ser Leu Arg Ala Asp Ala Val Ala His Leu Glu Ala Gly Lys Asp Tyr		
740	745	750
Leu Glu Ile Glu Val Gly Gly Arg Arg Leu Phe Phe Val Lys Ala His		
755	760	765
Val Arg Glu Ser Leu Leu Ser Ile Leu Leu Arg Asp Trp Leu Ala Met		
770	775	780
Arg Lys Gln Ile Arg Ser Arg Ile Pro Gln Ser Ser Pro Glu Glu Ala		
785	790	795
800		
Val Leu Leu Asp Lys Gln Gln Ala Ala Ile Lys Val Val Cys Asn Ser		
805	810	815
Val Tyr Gly Phe Thr Gly Val Gln His Gly Leu Leu Pro Cys Leu His		
820	825	830
Val Ala Ala Thr Val Thr Ile Gly Arg Glu Met Leu Leu Ala Thr		
835	840	845
Arg Glu Tyr Val His Ala Arg Trp Ala Ala Phe Glu Gln Leu Leu Ala		
850	855	860

Asp Phe Pro Glu Ala Ala Asp Met Arg Ala Pro Gly Pro Tyr Ser Met
 865 870 875 880
 Arg Ile Ile Tyr Gly Asp Thr Asp Ser Ile Phe Val Leu Cys Arg Gly
 885 890 895
 Leu Thr Ala Ala Gly Leu Thr Ala Val Gly Asp Lys Met Ala Ser His
 900 905 910
 Ile Ser Arg Ala Leu Phe Leu Pro Pro Ile Lys Leu Glu Cys Glu Lys
 915 920 925
 Thr Phe Thr Lys Leu Leu Ile Ala Lys Lys Lys Tyr Ile Gly Val
 930 935 940
 Ile Tyr Gly Gly Lys Met Leu Ile Lys Gly Val Asp Leu Val Arg Lys
 945 950 955 960
 Asn Asn Cys Ala Phe Ile Asn Arg Thr Ser Arg Ala Leu Val Asp Leu
 965 970 975
 Leu Phe Tyr Asp Asp Thr Val Ser Gly Ala Ala Ala Leu Ala Glu
 980 985 990
 Arg Pro Ala Glu Glu Trp Leu Ala Arg Pro Leu Pro Glu Gly Leu Gln
 995 1000 1005
 Ala Phe Gly Ala Val Leu Val Asp Ala His Arg Arg Ile Thr Asp
 1010 1015 1020
 Pro Glu Arg Asp Ile Gln Asp Phe Val Leu Thr Ala Glu Leu Ser
 1025 1030 1035
 Arg His Pro Arg Ala Tyr Thr Asn Lys Arg Leu Ala His Leu Thr
 1040 1045 1050
 Val Tyr Tyr Lys Leu Met Ala Arg Arg Ala Gln Val Pro Ser Ile
 1055 1060 1065
 Lys Asp Arg Ile Pro Tyr Val Ile Val Ala Gln Thr Arg Glu Val
 1070 1075 1080
 Glu Glu Thr Val Ala Arg Leu Ala Ala Leu Arg Glu Leu Asp Ala
 1085 1090 1095
 Ala Ala Pro Gly Asp Glu Pro Ala Pro Pro Ala Ala Leu Pro Ser
 1100 1105 1110
 Pro Ala Lys Arg Pro Arg Glu Thr Pro Ser Pro Ala Asp Pro Pro
 1115 1120 1125
 Gly Gly Ala Ser Lys Pro Arg Lys Leu Leu Val Ser Glu Leu Ala
 1130 1135 1140
 Glu Asp Pro Ala Tyr Ala Ile Ala His Gly Val Ala Leu Asn Thr
 1145 1150 1155
 Asp Tyr Tyr Phe Ser His Leu Leu Gly Ala Ala Cys Val Thr Phe
 1160 1165 1170
 Lys Ala Leu Phe Gly Asn Asn Ala Lys Ile Thr Glu Ser Leu Leu
 1175 1180 1185

Lys Arg Phe Ile Pro Glu Val Trp His Pro Pro Asp Asp Val Ala
 1190 1195 1200
 Ala Arg Leu Arg Thr Ala Gly Phe Gly Ala Val Gly Ala Gly Ala
 1205 1210 1215
 Thr Ala Glu Glu Thr Arg Arg Met Leu His Arg Ala Phe Asp Thr
 1220 1225 1230
 Leu Ala
 1235
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 Ala Arg Ala Ala Ser Gly Phe Phe Ala Pro Ala Gly Pro Arg Gly Ala
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 Gly Arg Gly Pro Pro Pro Cys Leu Arg Gln Asn Phe Tyr Asn Pro Tyr
 35 40 45
 Leu Ala Pro Val Gly Thr Gln Gln Lys Pro Thr Gly Pro Thr Gln Arg
 50 55 60
 His Thr Tyr Tyr Ser Glu Cys Asp Glu Phe Arg Phe Ile Ala Pro Arg
 65 70 75 80
 Val Leu Asp Glu Asp Ala Pro Pro Glu Lys Arg Ala Gly Val His Asp
 85 90 95
 Gly His Leu Lys Arg Ala Pro Lys Val Tyr Cys Gly Gly Asp Glu Arg
 100 105 110
 Asp Val Leu Arg Val Gly Ser Gly Gly Phe Trp Pro Arg Arg Ser Arg
 115 120 125
 Leu Trp Gly Gly Val Asp His Ala Pro Ala Gly Phe Asn Pro Thr Val
 130 135 140
 Thr Val Phe His Val Tyr Asp Ile Leu Glu Asn Val Glu His Ala Tyr
 145 150 155 160
 Gly Met Arg Ala Ala Gln Phe His Ala Arg Phe Met Asp Ala Ile Thr
 165 170 175
 Pro Thr Gly Thr Val Ile Thr Leu Leu Gly Leu Thr Pro Glu Gly His
 180 185 190
 Arg Val Ala Val His Val Tyr Gly Thr Arg Gln Tyr Phe Tyr Met Asn
 195 200 205
 Lys Glu Glu Val Asp Arg His Leu Gln Cys Arg Ala Pro Arg Asp Leu
 210 215 220

Cys Glu Arg Met Ala Ala Ala Leu Arg Glu Ser Pro Gly Ala Ser Phe
 225 230 235 240
 Arg Gly Ile Ser Ala Asp His Phe Glu Ala Glu Val Val Glu Arg Thr
 245 250 255
 Asp Val Tyr Tyr Tyr Glu Thr Arg Pro Ala Leu Phe Tyr Arg Val Tyr
 260 265 270
 Val Arg Ser Gly Arg Val Leu Ser Tyr Leu Cys Asp Asn Phe Cys Pro
 275 280 285
 Ala Ile Lys Lys Tyr Glu Gly Gly Val Asp Ala Thr Thr Arg Phe Ile
 290 295 300
 Leu Asp Asn Pro Gly Phe Val Thr Phe Gly Trp Tyr Arg Leu Lys Pro
 305 310 315 320
 Gly Arg Asn Asn Thr Leu Ala Gln Pro Arg Ala Pro Met Ala Phe Gly
 325 330 335
 Thr Ser Ser Asp Val Glu Phe Asn Cys Thr Ala Asp Asn Leu Ala Ile
 340 345 350
 Glu Gly Gly Met Ser Asp Leu Pro Ala Tyr Lys Leu Met Cys Phe Asp
 355 360 365
 Ile Glu Cys Lys Ala Gly Gly Glu Asp Glu Leu Ala Phe Pro Val Ala
 370 375 380
 Gly His Pro Glu Asp Leu Val Ile Gln Ile Ser Cys Leu Leu Tyr Asp
 385 390 395 400
 Leu Ser Thr Thr Ala Leu Glu His Val Leu Leu Phe Ser Leu Gly Ser
 405 410 415
 Cys Asp Leu Pro Glu Ser His Leu Asn Glu Leu Ala Ala Arg Gly Leu
 420 425 430
 Pro Thr Pro Val Val Leu Glu Phe Asp Ser Glu Phe Glu Met Leu Leu
 435 440 445
 Ala Phe Met Thr Leu Val Lys Gln Tyr Gly Pro Glu Phe Val Thr Gly
 450 455 460
 Tyr Asn Ile Ile Asn Phe Asp Trp Pro Phe Leu Leu Ala Lys Leu Thr
 465 470 475 480
 Asp Ile Tyr Lys Val Pro Leu Asp Gly Tyr Gly Arg Met Asn Gly Arg
 485 490 495
 Gly Val Phe Arg Val Trp Asp Ile Gly Gln Ser His Phe Gln Lys Arg
 500 505 510
 Ser Lys Ile Lys Val Asn Gly Met Val Asn Ile Asp Met Tyr Gly Ile
 515 520 525
 Ile Thr Asp Lys Ile Lys Leu Ser Ser Tyr Lys Leu Asn Ala Val Ala
 530 535 540
 Glu Ala Val Leu Lys Asp Lys Lys Lys Asp Leu Ser Tyr Arg Asp Ile
 545 550 555 560

Pro Ala Tyr Tyr Ala Ala Gly Pro Ala Gln Arg Gly Val Ile Gly Glu
 565 570 575
 Tyr Cys Ile Gln Asp Ser Leu Leu Val Gly Gln Leu Phe Phe Lys Phe
 580 585 590
 Leu Pro His Leu Glu Leu Ser Ala Val Ala Arg Leu Ala Gly Ile Asn
 595 600 605
 Ile Thr Arg Thr Ile Tyr Asp Gly Gln Gln Ile Arg Val Phe Thr Cys
 610 615 620
 Leu Leu Arg Leu Ala Asp Gln Lys Gly Phe Ile Leu Pro Asp Thr Gln
 625 630 635 640
 Gly Arg Phe Arg Gly Gly Gly Glu Ala Pro Lys Arg Pro Ala Ala
 645 650 655
 Ala Arg Glu Asp Glu Glu Arg Pro Glu Glu Gly Glu Asp Glu Asp
 660 665 670
 Glu Arg Glu Glu Gly Gly Glu Arg Glu Pro Glu Gly Ala Arg Glu
 675 680 685
 Thr Ala Gly Arg His Val Gly Tyr Gln Gly Ala Arg Val Leu Asp Pro
 690 695 700
 Thr Ser Gly Phe His Val Asn Pro Val Val Phe Asp Phe Ala Ser
 705 710 715 720
 Leu Tyr Pro Ser Ile Ile Gln Ala His Asn Leu Cys Phe Ser Thr Leu
 725 730 735
 Ser Leu Arg Ala Asp Ala Val Ala His Leu Glu Ala Gly Lys Asp Tyr
 740 745 750
 Leu Glu Ile Glu Val Gly Arg Arg Leu Phe Phe Val Lys Ala His
 755 760 765
 Val Arg Glu Ser Leu Leu Ser Ile Leu Leu Arg Asp Trp Leu Ala Met
 770 775 780
 Arg Lys Gln Ile Arg Ser Arg Ile Pro Gln Ser Ser Pro Glu Glu Ala
 785 790 795 800
 Val Leu Leu Asp Lys Gln Gln Ala Ala Ile Lys Val Val Cys Asn Ser
 805 810 815
 Val Tyr Gly Phe Thr Gly Val Gln His Gly Leu Leu Pro Cys Leu His
 820 825 830
 Val Ala Ala Thr Val Thr Ile Gly Arg Glu Met Leu Leu Ala Thr
 835 840 845
 Arg Glu Tyr Val His Ala Arg Trp Ala Ala Phe Glu Gln Leu Leu Ala
 850 855 860
 Asp Phe Pro Glu Ala Ala Asp Met Arg Ala Pro Gly Pro Tyr Ser Met
 865 870 875 880
 Arg Ile Ile Tyr Gly Asp Thr Asp Ser Ile Phe Val Leu Cys Arg Gly

885	890	895
Leu Thr Ala Ala Gly Leu Thr Ala Val Gly Asp Lys Met Ala Ser His		
900	905	910
Ile Ser Arg Ala Leu Phe Leu Ser Pro Ile Lys Leu Glu Cys Glu Lys		
915	920	925
Thr Phe Thr Lys Leu Leu Ile Ala Lys Lys Lys Tyr Ile Gly Val		
930	935	940
Ile Tyr Gly Gly Lys Met Leu Ile Lys Gly Val Asp Leu Val Arg Lys		
945	950	955
Asn Asn Cys Ala Phe Ile Asn Arg Thr Ser Arg Ala Leu Val Asp Leu		
965	970	975
Leu Phe Tyr Asp Asp Thr Val Ser Gly Ala Ala Ala Leu Ala Glu		
980	985	990
Arg Pro Ala Glu Glu Trp Leu Ala Arg Pro Leu Pro Glu Gly Leu Gln		
995	1000	1005
Ala Phe Gly Ala Val Leu Val Asp Ala His Arg Arg Ile Thr Asp		
1010	1015	1020
Pro Glu Arg Asp Ile Gln Asp Phe Val Leu Thr Ala Glu Leu Ser		
1025	1030	1035
Arg His Pro Arg Ala Tyr Thr Asn Lys Arg Leu Ala His Leu Thr		
1040	1045	1050
Val Tyr Tyr Lys Leu Met Ala Arg Arg Ala Gln Val Pro Ser Ile		
1055	1060	1065
Lys Asp Arg Ile Pro Tyr Val Ile Val Ala Gln Thr Arg Glu Val		
1070	1075	1080
Glu Glu Thr Val Ala Arg Leu Ala Ala Leu Arg Glu Leu Asp Ala		
1085	1090	1095
Ala Ala Pro Gly Asp Glu Pro Ala Pro Pro Ala Ala Leu Pro Ser		
1100	1105	1110
Pro Ala Lys Arg Pro Arg Glu Thr Pro Leu His Ala Asp Pro Pro		
1115	1120	1125
Gly Gly Ala Ser Lys Pro Arg Lys Leu Leu Val Ser Glu Leu Ala		
1130	1135	1140
Glu Asp Pro Ala Tyr Ala Ile Ala His Gly Val Ala Leu Asn Thr		
1145	1150	1155
Asp Tyr Tyr Phe Ser His Leu Leu Gly Ala Ala Cys Val Thr Phe		
1160	1165	1170
Lys Ala Leu Phe Gly Asn Asn Ala Lys Ile Thr Glu Ser Leu Leu		
1175	1180	1185
Lys Arg Phe Ile Pro Glu Val Trp His Pro Pro Asp Asp Val Ala		
1190	1195	1200

Ala Arg Leu Arg Ala Ala Gly Phe Gly Ala Val Gly Ala Gly Ala
1205 1210 1215

Thr Ala Glu Glu Thr Arg Arg Met Leu His Arg Ala Phe Asp Thr
1220 1225 1230

Leu Ala
1235